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"PANCYTOPENIA : CLINICAL AND ETIOLOGICAL PROFILE IN TERTIARY CARE HOSPITAL"

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"PANCYTOPENIA: CLINICAL AND ETIOLOGICAL PROFILE IN TERTARY CARE HOSPITAL"** is a bonafide work performed by **Dr.NOKCHUR IMCHEN,** post graduate student, Institute of Internal Medicine, Madras Medical College, Chennai-03, under our guidance and supervision in partial fulfilment of regulations of the Tamil Nadu Dr.M.G.R Medical University for the award of M.D. Degree Branch I (General Medicine) during the academic period from2016 to 2019.

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DECLARATION

I solemnly declare that the dissertation entitled **"PANCYTOPENIA: CLINICAL AND ETIOLOGICAL PROFILE IN TERTARY CARE HOSPITAL"** was prepared by me at Madras Medical College, Chennai, during August 2017 to January 2018 under the guidance and supervision of **Prof.Dr.VASANTHI.,M.D**, Institute of Internal Medicine, Madras Medical College, Chennai.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the University regulations for the award of the degree of M.D. Branch I (General Medicine).

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CONTENTS

ABBREVIATIONS

AML	-	Acute Myeloid Leukemia
ALG	-	Anti lymphocytic globulin
ALL	-	Acute Lymphoblastic Leukemia
ANA	-	Anti Nuclear Antigen
CTD	-	Connective Tissue Disease
FSH	-	Follicle Stimulating Hormone
G-CSF	-	Granulocyte Colony Stimulating factor
GM – CSF	-	Granulocyte Monocyte colony Stimulating factor
GVHD	-	Graft Versus Host Disease
HAART	-	Highly Active Anti Retro viral Therapy
CLD	-	Chronic Liver Disease
HBV	-	Hepatitis B Virus
HCV	-	Hepatitis C Virus
HIV	-	Human Immuno Deficiency Virus
HLA	-	Human Leucocyte Antigen
LFT	-	Liver Function Test
LDH	-	Lactate Dehydrogenase
LH	-	Leutenising Hormone
MCV	-	Mean Corpuscular Volume
MCH	-	Mean Corpuscular Hemoglobin

MCHA	-	Microcytic Hypochromic Anaemia
MCHC	-	Mean Corpuscular Haemoglobin Concentration
MDS	-	Myelodysplastic Syndrome
NCNC	-	Normocytic normochromic
PCV	-	Packed Cell Volume
PHT	-	Portal Hypertension
TSH	-	Thyroid Stimulating Hormone
TLC	-	Total Leucocyte Count
SLE	-	Systemic Lupus Erythematosus

INTRODUCTION

AIMS & OBJECTIVES

OF THE STUDY

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INTRODUCTION

Cytopenia is a disorder due to decreased production or cessation of one or more of the three blood cells[1] . Pancytopenia refers to reduction in all three formed elements of blood- erythrocytes, leucocytes and platelets[2]. It is not a disease entity, but rather a triad of findings that may result from a number of disease processes.

Pancytopenia can be a striking feature of many serious and life-threatening illnesses that may range from simple drug induced bone marrow hypoplasia, megaloblastic marrow, hypersplenism to fatal bone marrow aplasias and leukemias[3]. Megaloblastic anaemia, either due to Vitamin B12 or Folate deficiency, or both, seem to be an important cause in developing countries[4,5,6] while aplastic anaemia is a major cause in developed nations.[7]

The incidence of disorders causing pancytopenia varies depending on geographic distribution, genetic factors, nutritional status and the prevalence of infective disorders. Also the prognosis depends on both, the severity of pancytopenia and on the nature of underlying condition[8].

Clinically the presenting symptoms are usually attributable to anaemia or thrombocytopenia. Leucopenia is not a common cause of initial presentation, but can be the most serious threat to life during subsequent course of disorder[9,10].

Careful assessment of the blood film is important if the cause for the pancytopenia is not clinically apparent[11]. Physical findings and peripheral blood picture provide valuable information in the work up of patients and help in planning investigations and the need for bone marrow samples[12] .

Pancytopenia is an important clinico - haematological entity encountered in our day-to-day clinical practice. This study aims to evaluate the clinical presentation and etiological spectrum of pancytopenia admitted in our tertiary health centre.

AIMS AND OBJECTIVES OF THE STUDY

1) To study clinical profiles of patients with pancytopenia.
2) To study the underlying etiology of pancytopenia.

REVIEW OF LITERATURE

DEFINITION:

Pancytopenia is defined as reduction of all the three formed elements of blood namely erythrocytes, leucocytes and platelets below the normal reference range[1] . Anaemia is defined as haemoglobin level less than 13g/dl in men and 12g/dl in women, according to WHO. Thrombocytopenia is a platelet count less than 150,000 per microliter and leucopenia is a white blood cell count less than 4,000 per microliter. Although leucopenia may be caused by lymphopenia or neutropenia, the most common finding is neutropenia with an absolute neutrophil count less than 1,500 per microliter.

HISTORY OF PANCYTOPENIA:

Hemopoiesis, the production of blood cells is a fundamental concept in haematology. In the eighteenth century, Neumann and Bizzozero established the relationship between blood and the bone marrow. In 1868, Neumann noted that bone marrow was an important organ for the formation of red blood cells[2] . Literature regarding aplastic anaemia and fanconi anaemia are much available than various other causes of pancytopenia. In 1888, Dr.Paul Enrilch gave the earliest case description of aplastic anaemia where he described a young woman who died following an abrupt illness that manifested as severe anaemia, bleeding, hyperpyrexia and a markedly hypocellular marrow[13]. In 1904, the term aplastic anaemia was introduced by Chaufford[13]. Aplastic anaemia, a disease due to the absence of hemopoiesis has had a parallel history

since the discovery of the function of bone marrow in the mid nineteenth century. In 1927, Guido Fanconi first reported Familial syndrome of pancytopenia and congenital physical abnormalities. Fanconi described three brothers, who had pancytopenia as well as physical abnormalities; he called their macrocytic anaemia “perniziosiforme”[1]. Naegeli suggested in 1931 that the term Fanconi anaemia be used for familial aplastic anaemia and congenital physical anomalies[1] . Environmental influences and nutritional causes of pancytopenia were accounted only in the late 20th century.

STUDIES ON PANCYTOPENIA:

In literature, various studies are available, that suggests cytopenias as manifestations of various systemic disorders. Various studies throughout the world have reported the commonest cause of pancytopenia as aplastic anaemia [3]. The International Aplastic Anaemia and Agranulocytosis Study(IAAAS) conducted a prospective study between 1980 and 1984 in Europe and Israel which showed the overall incidence as 2 cases per 1 million people ;however the incidence is 3 fold in southeast asia[10].

In Indian scenario, various studies conducted revealed a nutritional disorder, megaloblastic anaemia as the commonest cause of pancytopenia. A largest study conducted by Khunger et al included 200 cases of pancytopenia and concluded megaloblastic anaemia as the commonest cause which accounted to 72%[15]. In another study by Kumar et al done over a period of 6 years which included 191 cases, megaloblastic anaemia accounted for about

39% of cases[12]. Yet, in a recent study by Thilak et al, megaloblastic anaemia was proved to be the commonest cause and also revealed few interesting and rare causes of pancytopenia like drug induced agranulocytosis, waldenstroms macroglobulinemia[3]

By 1934, aplastic anaemia, although still not clearly defined, was described as a distinct clinical entity characterized by pancytopenia and thought to be the result of depressed bone marrow activity[1] . A study by Khunger, Morley A et al, of lymphocytes from eleven patients with aplastic anaemia, suggested that in 7 patients the DNA was abnormal and,it was hence concluded that in aplastic anaemia, DNA damage in stem cells may lead to a failure of proliferation[15] . In the late 1960s , Mathe et al was among the first to postulate an autoimmune basis for aplastic anaemia [16][17].

Aplastic anaemia being the most common cause of pancytopenia worldwide, many studies are available in the literature accounting for their etiology. Idiopathic aplastic anaemia accounts for more than 70% cases of paediatric anaemia after ruling out other possible etiology[18]. Also Chloramphenicol, a broad spectrum antibiotic introduced in 1949 was also found to cause a dose dependent suppression of hemopoiesis, particularly erythropoesis, through its action on mitochondrial DNA[19].

Infective cause of pancytopenia has also been described in a child with hereditary spherocytosis who acquired human parvovirus B19 infection developed transient pancytopenia[20]. Seronegative hepatitis precedes the

diagnosis of aplastic anaemia in 3 to 5% of cases and is recognized as hepatitis associated aplastic anaemia[21].

A Leukemia Research Fund (LRF) -UK based study puts the annual incidence of MDS as 3.6 per 100000[22] . One group has suggested a prevalance of 1 in 500 in those who presented with pancytopenia[23]. In a clinical study in 33 children with primary myelodysplastic syndrome (MDS), it was noted that the predominant presenting feature was pancytopenia[24]. Also,in a study of the haematological spectrum of myelodysplastic syndrome in 31 cases, pancytopenia constituted 16.1%[25].

HEMATOPOIESIS[26]

This is the process of production of the formed elements of the blood. The process takes place in the bone marrow. It initially begins from a single type of cell called the pluripotential hematopoietic stem cell, from which all the cells of the circulating blood are eventually derived.

Although these cells reproduce, a small portion of them is retained in the bone marrow exactly like the original pluripotential cells but their numbers tends to diminish with age. However, most of the reproduced cells differentiate to form the other cell types.

The intermediate stage cells, called committed stem cells become committed to a particular line of cells and are very much like the pluripotential stem cells.

The different committed stem cells, are capable of producing colonies of specific types of blood cells when grown in culture.

A committed stem cell that produces erythrocytes is called a colony-forming unit–erythrocyte(CFU-E) and those that form granulocytes and monocytes have the designation CFU-GM.

Growth and reproduction of the different stem cells are controlled by multiple proteins called growth inducers. Four major growth inducers have been described, they promote growth but not differentiation of the cells. Interleukin-3, promotes growth and reproduction of virtually all the different types of committed stem cells, whereas the others induce growth of only specific types of cells. Another set of proteins called differentiation inducer causes one type of committed stem cell to differentiate one or more steps toward a final adult blood cell.

Formation of the growth and differentiation inducers in turn is controlled by factors outside of the bone marrow. For instance, exposure of the blood to low oxygen for a long time results in growth induction, differentiation, and production of erythrocytes(RBCs). Similarly, infectious diseases cause growth, differentiation, and of specific types of white blood cells(WBCs) that are needed to combat infection.

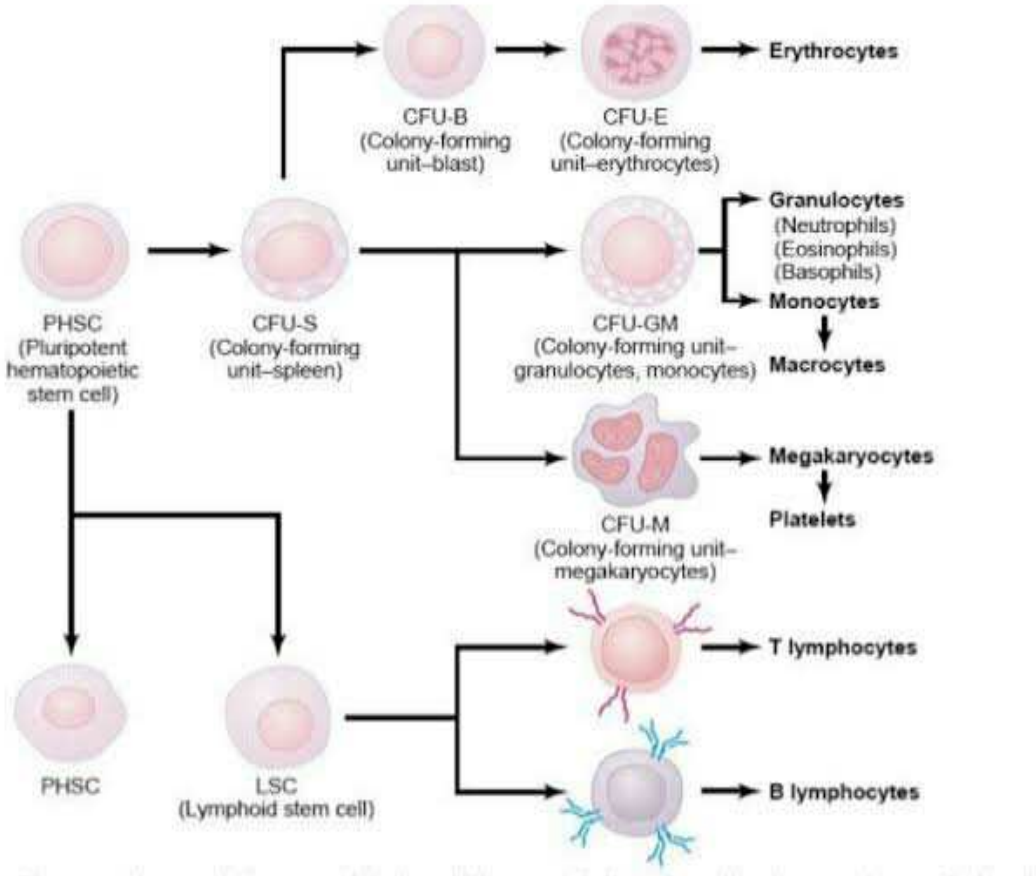


Figure: Formation of different blood cells from Pluripotent hematopoietic stem cell in the Bone marrow

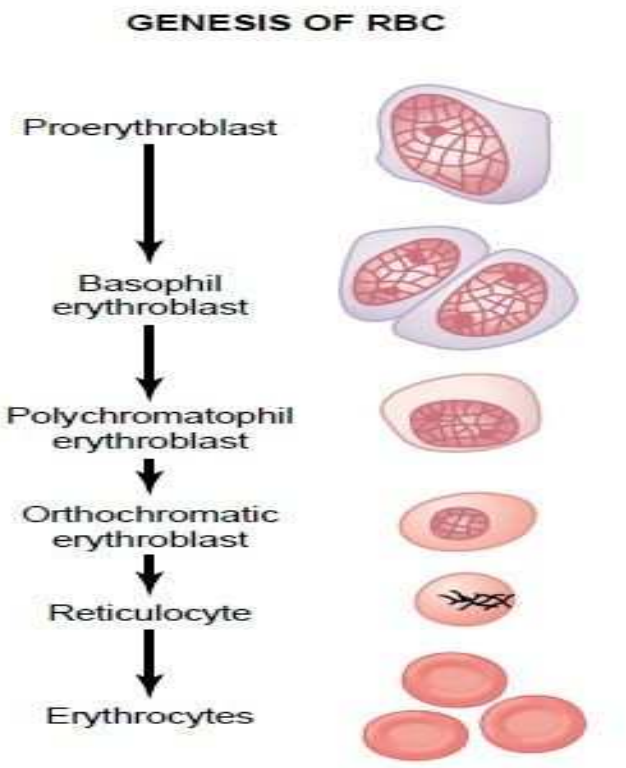


Figure: Genesis of normal Red blood cells.

ETIOLOGY[27]

Pancytopenia with Hypocellular Bone Marrow

Acquired aplastic anaemia

Constitutional aplastic anaemia (Fanconi's anaemia, dyskeratosis congenita)

Some of the myelodysplasias

Rare aleukemic leukemia (AML)

Some cases of acute lymphoid leukemia

Some cases of lymphomas of bone marrow

Pancytopenia with Cellular Bone Marrow

Primary bone marrow diseases/disorders

Myelodysplasia

Paroxysmal nocturnal hemoglobinuria

Myelofibrosis

Some aleukemic leukemia Myelophthisis

Bone marrow lymphoma

Hairy cell leukemia

Secondary to systemic diseases

Systemic lupus erythematosus

Hypersplenism

Vitamin B12, folate deficiency

Overwhelming infection

Alcohol

Brucellosis

Sarcoidosis

Tuberculosis

Leishmaniasis

Hypocellular Bone Marrow +/- Cytopenia

Q fever

Legionnaires' disease

Anorexia nervosa, starvation

Mycobacteria

PATHOPHYSIOLOGY OF PANCYTOPENIA:

There are various mechanisms by which pancytopenia develops.

1. Conditions associated with a decrease in hematopoietic cell production in bone marrow as a result of;

   a) Destruction of marrow tissue by toxins (acellular or hypoplastic marrow).

   b) Replacement by abnormal or malignant tissue.

   c) Suppression of normal marrow growth and differentiation.

2. Conditions in which the marrow may be normally cellular or even hypercellular, and no abnormal cells may be present. The mechanisms are -

   a) Ineffective hematopoiesis with cell death in the marrow.

   b) Formation of defective cells that are rapidly removed from the circulation.

c) Trapping of normal cells in hypertrophied and overactive reticuloendotheliall system.

d) Sequestration and/or destruction of cells by action of antibodies.

CLINICAL FEATURES OF PANCYTOPENIA:

The clinical manifestations depending on the severity of anaemia, leucopenia, and thrombocytopenia[9]. Initial presenting symptoms are usually attributable to anaemia and include mild progressive weakness, fatigue and exertional dyspnea but symptoms maybe initially subtle hence is neglected by the patient. However,elderly patients may present abruptly with heart failure symptoms. Those with neutropenia are predisposed to various infections and presents with unexplained high fevers, rigor and repeated, persistent infections while thrombocytopenia manifest as haemorrhage from skin, nose, and gums. Those with severe thrombocytopenia may present with signs and symptoms of retinal haemorrhage and even life-threatening intra-cranial bleed.

A detailed history may shed a light into the etiological diagnosis of pancytopenia. History of gastrectomy or ileal resection suggests the possibility of vitamin B12 deficiency; history of previous drug intake and cancer therapy may suggest drug-induced aplastic anaemia; dark colored early morning urine suggests paroxysmal nocturnal hemoglobinuria. Family history may give clue to the inherited forms of aplastic anaemias. Personal history like vegan diet, alcohol consumption must be entertained and promiscuous behaviour for the

possibility of HIV should be enquired. Travel history must also be included to rule out infectious causes.

Physical examination may reveal fever, pallor, 14etechiae and ecchymotic patches over the skin, mucous membranes and conjunctiva[9]. Presence of splenomegaly and lymphadenopathy should alert the clinician of the possibility of leukemia, lymphoma, myelofibrosis and various storage diseases. On the other hand, lack of these signs as well as lack of evidence of vitamin B12 or folate deficiency should suggest multiple myeloma or aplastic anaemia. Diarrhoea, jaundice and weight loss are other possible but rare presentation[2].

MEGALOBLASTIC ANEMIA [27, 28, 29, 30]

The megaloblastic anaemias are disorders caused by impaired DNA synthesis. Those cells having relatively rapid turnover, especially hematopoietic precursors and gastrointestinal epithelial cells are primarily affected. Eventhough the cell division is sluggish, cytoplasmic development progresses normally, so it results in formation of megaloblastic cells which tends to be large, with an increased ratio of RNA to DNA . The presence of megaloblastic cells is the morphologic hallmark. These megaloblastic erythroid progenitors tend to be destroyed in the marrow, a process known ineffective erythropoiesis.

Megaloblastic anaemia most commonly results from folate or cobalamin (vitamin B12 deficiency).

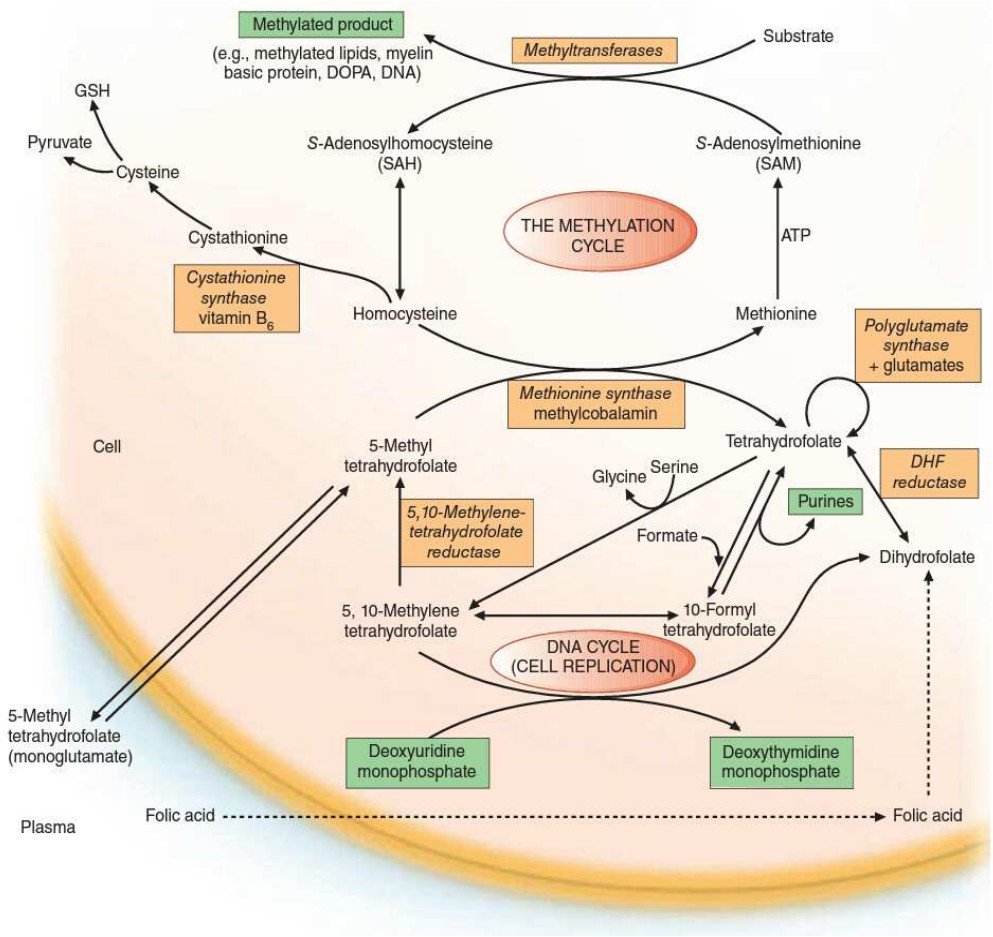


Figure: The role of Folates in DNA synthesis, DHF-Dihydrofolate, GSH-Glutathione

ETIOLOGY OF MEGALOBLASTIC ANAEMIA

Cobalamine deficiency

I. Inadequate intake – Vegetarians

II. Malabsorption

A) Defective release of Cobalamin from food

1. Gastric achlorhydria

2. Partial gastrectomy

3. Drugs that block acid secretion

B) Inadequate production of intrinsic factor (IF)

1. Pernicious anaemia

2. Total Gastrectomy

3. Congenital absence or functional abnormality of IF (rare)

C) Disorders of terminal ileum

1. Tropical sprue
2. Non-tropical sprue
3. Regional enteritis
4. Intestinal resection
5. Neoplasm and granulomatous disorder (rare)

D) Competition for Cobalamin

1. Fish Tapeworm (Diphyllobothrium latum)

2. Bacteria: “blind loop” syndrome

E) Drugs: p-amino salicyclic acid, colchicines, neomycin

III. Others

A) Nitrous oxide

B) Congential enzyme defect

Folic acid deficiency

I. Inadequate intake: Unbalanced diet (common in alcoholics, teenagers)

II. Increased requirements

A) Pregnancy

B) Infancy

C) Malignancy

D) Increased hematopoiesis

E) Chronic exfoliative skin disorders

F) Hemodialysis

III. Malabsorption

A) Tropical sprue

B) Non-tropical sprue

C) Drugs: Phenytoin, barbiturate, (?) ethanol

IV. Impaired metabolism

A) Inhibitors of dihydrofolate reductase: methotrexate, pyrimethamine, triamterene, pentamidine.

B) Alcohol

Other causes

I. Drugs that impair DNA metabolism

A) Purine antagonists: 6-mercaptopurine , azathioprine, etc.

B) Pyrimidine antagonists: 5-flurouracil, cytosine arabinoside etc.

C) Others: Procarbazine, hydroxyurea, acyclovir, zidovudin

II. Metabolic disorders

A) Hereditary orotic aciduria

B) Lesch-Nyhan syndrome

III. Megaloblastic anaemia of unknown etiology

A) Refractory megaloblastic anaemia

B) Di Guglielmos syndrome

C) Congenital dyserythropoietic anaemia

CLINICAL FEATURES:

COBALAMIN DEFICIENCY

Pernicious anaemia (PA) is the most common cause of cobalamin deficiency. It is a condition in which the portion of gastric mucosa that contains the parietal cells is destroyed through an autoimmune mechanism. The clinical features of cobalamin deficiency may manifest as hematological, gastrointestinal, and the neurological features. The hematologic manifestations are almost entirely the result of anaemia and include weakness, light-headedness, vertigo and tinnitus, as well as palpitation, angina and in severe cases, symptoms of congestive failure. Very rarely purpura may appear, due to presence of thrombocytopenia. On examination, the patient maybe pale, with slight yellowish discoloration of skin and eyes. The gastrointestinal manifestations are glossitis in which the tongue appears smooth and beefy red, anorexia with moderate weight loss, and diarrhoea.

Apart from causing megaloblastic anaemia, cobalamin deficiency also cause a demyelinating disease, Sub-acute combined degeneration of the spinal cord (SACD) that manifests itself as peripheral neuropathy, spastic paralysis with ataxia. It may also manifest as dementia, psychosis, or a combination of the foregoing. Neurologic symptoms without anaemia as a result of "Subtle" cobalamin deficiency appears to be relatively widespread among the elderly.

FOLATE DEFICIENCY

Folate deficiency most often is nutritional but may also be seen in alcoholics, elderly and with patients on hyperalimentation or hemodialysis and in malabsorption syndromes such as tropical and nontropical sprue. The hematologic and gastrointestinal manifestations are the same as those of cobalamin deficiency. However, neurologic abnormalities do not occur. Diagnosis is based on serum folate levels, which provides information about the current level of folate, and in red cells,the folate levels over the preceeding 6 weeks. Nutritional folate deficiency is treated with folic acid.

LABORATORY FEATURES: [27]

Serum Cobalamin:

Normal serum levels range from 118-148 pmol/L(160-200ng/L) to ~738 pmol/L(1000ng/L). In patients with cobalamin deficiency the level is usually <74 pmol/L (100ng/L). Values between 74-148 pmol/L (100-200ng/L) are considered borderline.

Serum Folate:

Normal serum levels range from 11 nmol/L (2 microgram/L) to ~82 nmol/L (15 microgram/L). It reflects recent diet hence maybe low before there is hematologic or biochemical evidence of deficiency. Another valuable indicator of body folate stores is the Red cell folate which ranges fron 880-3520 microMol/L (160-640 microgram/L).

Peripheral smear:

All cell lines are affected. The blood smear demonstrates marked anisocytosis and poikilocytosis, together with macrovalocytes and in severe cases can show basophilic stippling and nuclear remnants (Cabot rings, and Howell-Jolly bodies). Erythroid activity in the marrow is enhanced, but with a decreased reticulocyte count as these megaloblastic cells are usually destroyed due to ineffective hematopoiesis. The morphologic changes in the red cells is proportional with the severity of anaemia. When the hematocrit is less than 20 percent, erythroblasts with megaloblastic nuclei, including an occasional promegaloblast, may appear in the blood. The presence of megaloblastic cells is the morphologic hallmark [mean corpuscular volume (MCV) = 100–150 fl or more]. The presence of coexisting iron deficiency, thalassemia trait, or inflammation can prevent macrocytosis. Slight macrocytosis often is the earliest sign of megaloblastic anaemia.

Neutrophils shows hypersegmented nuclei often more than the usual three to five lobes. Cells may contain six or more lobes. In nutritional megaloblastic anaemias hypersegmented neutrophils are an early sign of megaloblastosis and persist in the blood for many days after treatment. The presence of even a single hypersegmented neutrophil should warrant evaluation for megaloblastic anaemia. With specific therapy,these abnormalities gets corrected usually within 2 days, although some abnormalities may persist for months.

Platelets vary more widely in size (increased platelet distribution width). Bizarre and misshapen platelets may also be seen.

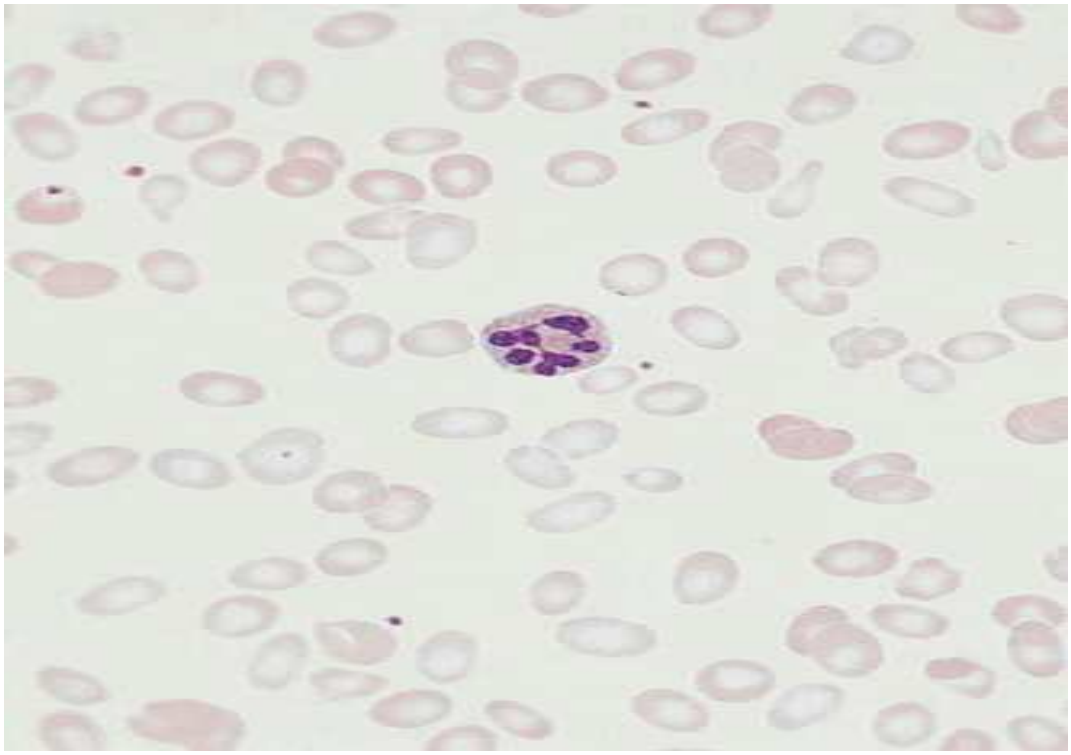


Figure: Peripheral smear finding of severe megaloblastic anaemia, hypersegmented neutrophils.

Bone Marrow:

The bone marrow is hypercellular with a decreased myeloid/erythroid ratio which may fall to 1:1 ratio or even lower. Erythroid precursors are abnormally large with nuclei that appears much less mature than would be expected from the development of the cytoplasm. The nuclear chromatin is more dispersed than expected, and it condenses in a peculiar fenestrated pattern. Granulocyte precursors are also affected, many being larger than normal, including meta-myelocytes. Megakaryocytes are decreased and show abnormal morphology.

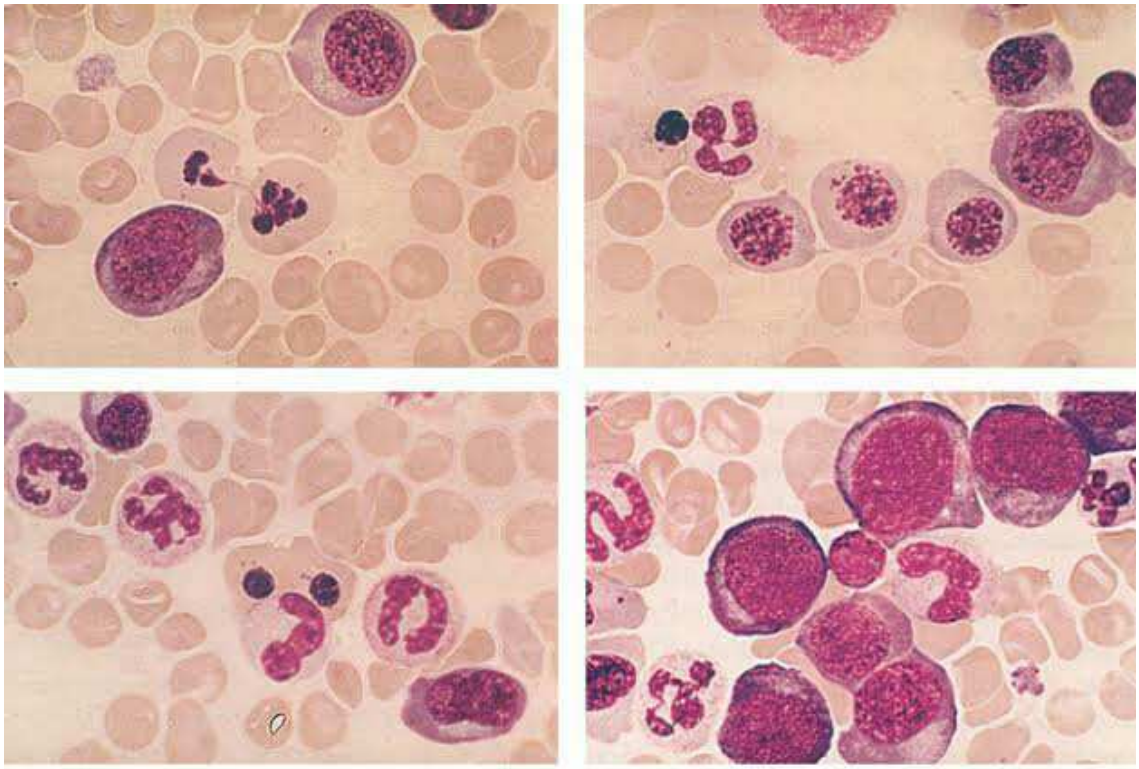


Figure: Bone marrow finding of severe megaloblastic anaemia

Others :

Enhanced intramedullary destruction of erythroblasts results in an increase in unconjugated bilirubin and lactic acid dehydrogenase in plasma.

Schilling test, although not performed routinely can be used to delineate the pathogenesis once cobalamin deficiency has been established.

TREATMENT [27]

The indications for starting cobalamin therapy are a well-documented megaloblastic anaemia or other hematologic abnormalities and neuropathy. Replenishment of body stores is achieved with 6 doses IM injection of 1000 microgram hydroxocobalamin given at 3 to 7 day intervals. A maintenance dose is given as 1000 microgram hydroxocobalamin once in every three months.

In pernicious anaemia, daily dose of 1000-2000 microgram is given orally.

For folate deficiency, a daily oral dose of 5-15mg folic acid is given and continued for about 4 months, when all folate-deficient reds cells would have been eliminated and replaced. Cobalamin deficiency should be excluded and corrected before large doses of folic acid are given, as cobalamin neuropathy may develop despite correction of anaemia.

APLASTIC ANEMIA [10]

Aplastic anaemia is defined as the failure of bone marrow to produce blood cell components.

Pancytopenia with Hypocellular marrow is the Hallmark feature. It is a rare entity and is again broadly classified into acquired and inherited cause of which the inherited forms are still rarer to encounter. Idiopathic aplastic anaemia accounts for approximately 65% of all cases which means that majority of cases are without known apparent cause.

PATHOPHYSIOLOGY

The pancytopenia in aplastic anaemia reflects failure/ damage to the hematopoietic cell compartment and manifests as a severe decrease in the numbers of all hematopoietic progenitor cells. Two mechanisms have been suggested for bone marrow failure. Cells bearing the CD34 antigen, which is a marker of early hematopoietic cell, are greatly diminished; and committed and primitive progenitor cells are virtually absent in functional studies. There are two possible proposed mechanism. The first is direct hematopoietic injury by chemicals (eg, benzene), drugs, or radiation to both proliferating and quiescent hematopoietic cells. The second mechanism, is immune-mediated suppression of marrow cells where increased numbers of activated cytotoxic T cells observed in aplastic anaemia patients decline with successful immuno-suppresive therapy. The latter is supported by clinical observations and laboratory studies.

Aplastic anaemia does not appear to result from defective stroma or growth factor production.

CLASSIFICATION OF APLASTIC ANAEMIA[27]

ACQUIRED

SECONDARY

- Drugs and chemicals

    -Regular effects (Cytotoxic agents, Benzene)

-Idiosyncratic reactions (Chloramphenicol, NSAIDs, Antiepileptics, Gold)

- Viruses

  -Ebstein barr virus (infectious mononucleosis)

  -Hepatitis(non-A,non-B,non-C)

  -Parvovirus B19

  -HIV-1

- Immune diseases

  -Eosinophilic fasciitis

  -Hyperimmunoglobulinemia

  -Large granular lymphocytosis (LGL)

  -Thymoma / thymic carcinoma

  -Graft versus Host disease in immunedeficiency

- Paroxysmal Nocturnal Hemoglobinuria (PNH)
- Pregnancy

IDIOPATHIC

INHERITED

- Fanconi anaemia
- Dyskeratosis Congenita
- Schwachman-Diamond syndrome
- Reticular dysgenesis
- Amegakaryocytic thrombocytopenia

- Familial Aplastic anaemia
- Preleukemia (monosomy 7,etc)
- Non-hematologic syndromes (Down,Dobowitz,Seckel)

CLINICAL FEATURES:

The onset of illness could be abrupt or have a more insidious course. Bleeding is the most common early symptom; the patient would have noticed days to weeks of easy bruising**,** petechiae, gum bleeds, epistaxis, and sometimes heavy menstrual flow. Symptoms of anaemia are also frequent, including lassitude, weakness, shortness of breath and a pounding sensation in the ears. Inspite of decreased white cell count, infection is an unusual first symptom. Thorough and detailed history taking is necessary to elicit drug use, chemical exposure and preceding viral illness.

Physical examination may show pallor of the skin and mucous membranes which is common. Petechiae and ecchymoses are often present, and retinal haemorrhages may be present. A striking feature of aplastic anaemia is the restriction of symptoms to the hematologic system; hepatosplenomegaly, lymphadenopathy, or bone pain is uncommon. Café au lait spots and short stature suggest Fanconi’s anaemia, peculiar nails suggest Dyskeratosis congenita.

LABORATORY STUDIES

BLOOD:

The smear shows large erythrocytes with paucity of platelets and granulocytes. Reticulocytes are absent or few, and lymphocyte numbers may be normal or reduced.

Mean corpuscular volume is usually increased.

BONE MARROW:

The hallmark of aplastic anaemia is pancytopenia and a hypocellular bone marrow. Bone marrow aspiration and biopsy must be performed to rule out other possible causes for pancytopenia, such as MDS or leukemia. The bone marrow is usually readily aspirated but appears dilute on smear, and the fatty biopsy specimen may be grossly pale on withdrawal. The biopsy is superior for determination of cellularity and shows mainly fat under the microscope, with hematopoietic cells occupying <25% of the marrow space. The residual hematopoietic cells have normal morphology except for mild megaloblastic erythrocytes.

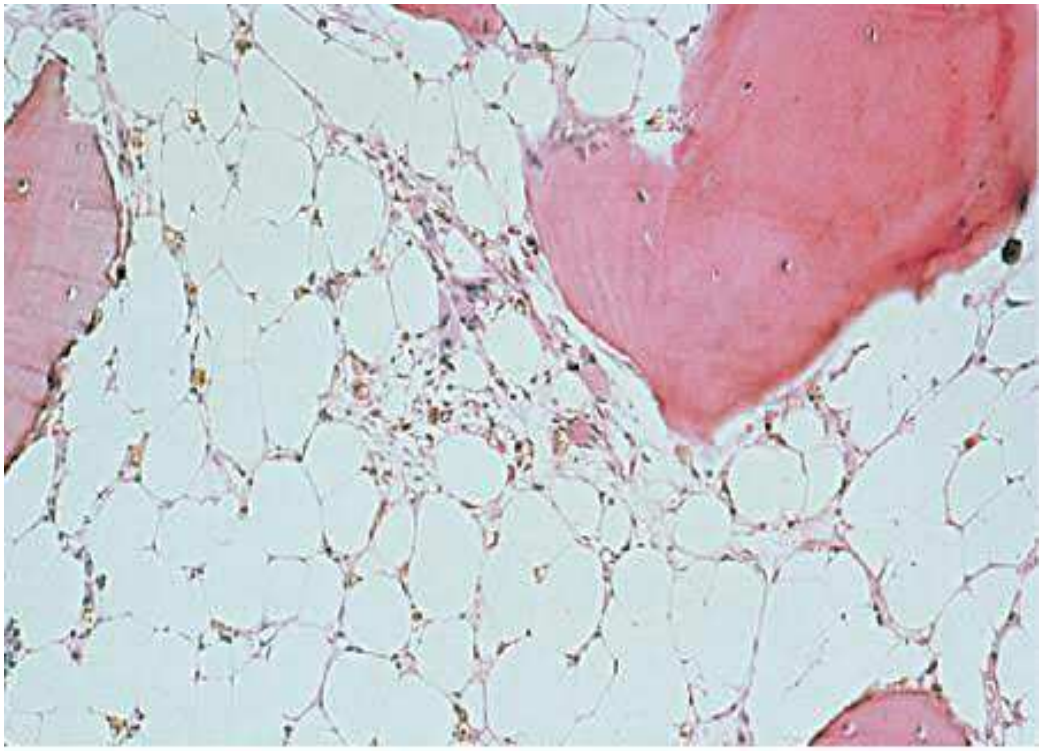


Figure: Bone marrow biopsy of Aplastic anaemia

ANCILLARY STUDIES:

Chromosome breakage studies of peripheral blood using diepoxybutane[DEB] or mitomycin C should be performed on children to exclude Fanconi's anaemia. Chromosomal studies of bone marrow cells are often diagnostic in myelodysplastic syndrome and negative in typical aplastic anaemia. Flow cytometric studies is a sensitive test for the diagnosis of PNH. Serological studies may show evidence of viral infection, especially Ebstein Barr virus and HIV but not for post hepatitis aplastic anaemia which is typically seronegative. Also, MRI to assess for marrow fat content can be used to differentiate Aplasia from MDS.

PROGNOSIS:

The major prognostic determinant is the blood count. Severe disease is defined by the presence of two or three parameters, absolute neutophil count <500/microL, platelet count <20,000/microL and corrected reticulocyte count< 1%. Survival of patients who fulfil these criteria is about 20% at one year after diagnosis.

TREATMENT:

Treatment aims at reversing the underlying marrow failure and provide supportive care. Careful search for correctable cause like exposures to drugs or chemicals should be made. Severe acquired aplastic anaemia can be cured by replacement of the absent hematopoietic cells by stem cell transplant, or ameliorated by suppression of the immune system to allow recovery of the patient's residual bone marrow function. Hematopoietic growth factors have limited usefulness and glucocorticoids are of no value as primary therapy.

Bone marrow transplantation:

This is the best therapy for the young patient with a fully histocompatible sibling donor. For allogenic transplant from fully matched siblings, long-term survival rates for children are about 90%. Transplant morbidity and mortality are increased among adults, due mainly to the increased rate of chronic graft-versus host disease and serious infections. For those without a suitable sibling donor, alternative donor transplant is used after

high-resolution matching at HLA, conditioning regimens and GVHD prophylaxis and has led to improved survival.

Immunosuppression:

The standard regimen is the combination of antithymocyte globulin(ATG) and cyclosporine. It induces hematologic recovery in about 60-70% of patients. The response is better in younger patients compared to older ones.

Horse ATG is given at 40mg/kg per day for four days, rabbit ALG is administered at 3.5 mg/kg per day for five days. Most patients are given methylprednisolone, 1 mg/kg per day for two weeks, to ameliorate the immune consequences of ATG. Cyclosporine is administered orally at an initial dose of 12 mg/kg per day in adults, with subsequent adjustment according to blood levels obtained every two weeks (150-200ng/mL).

Other therapies:

The effectiveness of androgen therapy has not been verified in controlled trials, but occasional patients showed response on continued therapy. For patients with moderate disease or those with severe pancytopenia who have failed immunosuppression, a 3 to 4 months trail is appropriate. Hematopoietic growth factors, G-CSF, GM-CSF and interleukin-3, are not definite therapy and their role is not clear in severe aplastic anaemia. Thrombopoietin mimetics by way of acting as a stem cell stimulant has shown blood count recovery in refractory cases.

Supportive care:

Most important is the control of infection and in the presence of severe neutropenia empiric broad spectrum antibiotic should be promptly initiated without waiting for culture reports.

Both platelet and erythrocyte numbers can be maintained by transfusion. Any rational regimen of prophylaxis requires transfusions once or twice weekly in order to maintain the platelet count >10,000/microL . Menstruation should be suppressed by oral estrogen or nasal LH/FSH antagonists. Red blood cells should be transfused to maintain a normal level of activity, usually at a hemoglobin value of 7g/dL (9g/dL if there is underlying cardiac or pulmonary disease), given as 2 units every 2 weeks (in patient without a functioning bone marrow). Iron chelators should be considered at the fiftieth transfusion to avoid secondary hemochromatosis.

HYPERSPLENISM

The term hypersplenism refers to exaggeration of the spleen's normal filtration and phagocytic functions. Hypersplenism usually is characterised by triad of splenomegaly, blood cytopenias, and compensatory marrow hyperplasia; and these abnormalities are characteristically corrected by splenectomy[31].

The disorder can occur primarily by enlargement of the spleen from vascular congestion, histiophagocytic hyperplasia, cellular infiltration, or secondarily by the inability of physically abnormal red cells, such as sickle

cells, or antibody-coated cells, such as in immune thrombocytopenia purpura, to navigate the circulation or avoid engulfment by the mononuclear phagocyte population of the normal spleen[32].

Pathophysiology:

Splenomegaly causes inappropriate sequestration of both normal and abnormal blood cells due increase blood channeled through the red pulp[33,34]. Spleen enlargement may result from expansion of the red pulp compartment in any red cell sequestration process; extramedullary hematopoiesis, notably in idiopathic myelofibrosis; hyperplasia or neoplasia involving the white pulp, such as infectious mononucleosis or lymphoma, respectively; or histiophagocytic hyperplasia.

The increased size of the filtering bed is more pronounced when the splenomegaly is caused by congestion than when it is caused by cellular infiltration. Nevertheless, even in these pathologic conditions splenomegaly may be associated with severe hypersplenic sequestration of normal cells. Splenomegaly increases the vascular surface area and thereby the marginated neutrophil pool[35,36]**.** Platelets are especially likely to be sequestered in an enlarged spleen, and up to 90 percent of the total number of platelets in blood may be found in massively enlarged spleens. However, sequestered white cells and platelets survive in the spleen and may be available when increased demand requires neutrophils or platelets, although their release may be slow[37].

Red cells are destroyed prematurely in the red pulp and anaemia has been considered to be the result of dilution of red cells in an expanded plasma volume. However, expansion as measured by radiolabeled albumin or fibrinogen, results more from an increase in the splenic pool of protein rather an increase in circulating plasma volume.

Varying amounts of erythrophagocytosis are present, reflecting the normal culling of senescent red cells. Erythrophagocytosis increases as a result of hemolytic anaemia and viral infections, and in alloimmunized transfusion recipients. Macrophages within the sinusoids contain red cell fragments. When the process is pronounced, the littoral cells become cuboidal and stand out on the basement membrane ("hobnails").

ETIOLOGY[38]

Splenomegaly with Appropriate Hypersplenism

Hereditary hemolytic anemias

Hereditary spherocytosis

Hereditary elliptocytosis

Thalassemia

Sickle cell anaemia (infants)

Autoimmune cytopenias

Idiopathic thrombocytopenia

Essential neutropenia

Acquired hemolytic anaemia

Infections and inflammations

Infectious mononucleosis

Subacute bacterial endocarditis

Miliary tuberculosis

Rheumatoid arthritis (Felty syndrome)

Lupus erythematosus

Sarcoidosis

Brucellosis

Leishmaniasis

Schistosomiasis

Malaria

Splenomegaly with Inappropriate Hypersplenism

Congestion (Banti syndrome)

Cirrhosis of the liver

Portal vein thrombosis

Splenic vein obstruction

Budd-Chiari syndrome

Congestive heart failure

Infiltrative disease

Leukemias

Chronic and acute Lymphomas

Polycythemia vera

Agnogenic myeloid metaplasia

Gaucher disease

Niemann-Pick disease

Glycogen storage disease

Amyloidosis

Laboratory Features:

The blood cell morphology usually is normal, although a few spherocytes may result from metabolic conditioning of red cells during repeated slow transits through the expanded red pulp. Reticulocyte count is increased due to compensatory increase in red cell production. However, the spleen preferentially sequesters reticulocytes hence this finding may be quantitatively less evident. There is also a compensatory increase in neutrophil or platelet production but is more difficult to identify morphologically. Tests

such as epinephrine mobilization have been used to distinguish sequestration from ineffective cellular production. Epinephrine releases neutrophils and platelets from the spleen, but the test may be difficult to interpret since epinephrine also releases the cells from marginal pools[39].

Treatment:

Splenectomy is the mainstay of treatment and produce partial or complete recovery of the abnormal blood picture in otherwise uncomplicated cases[40]. However, in asymptomatic cases of hypersplenism, splenectomy offers no benefit to the patient. Splenectomy is indicated when significant problems are caused by the sole or the additional effect of hypersplenism in reducing the count of blood cells, usually anaemia of sufficient severity to cause symptoms, neutropenia predisposing to infectious, or thrombocytopenia causing spontaneous bleeding.

MYELODYSPLASTIC SYNDROMES [27]

The myelodysplastic syndromes (MDS) are heterogenous group of hematologic disorders broadly characterised by both 1) cytopenias due to bone marrow failure and 2) a high risk of development of acute myeloid leukemia (AML). Anaemia often with thrombocytopenia and neutropenia occurs with dysmorphic and usually cellular bone marrow.

Idiopathic MDS is a disease of the elderly with mean age of onset of >70yrs with the incidence of 120->500 per million. However, secondary or therapy-related MDS is not age related.

WORLD HEALTH ORGANIZATION(WHO) CLASSIFICATION OF MYELODYSPLASTIC SYNDROMES[27]

1. Refractory cytopenias with unilineage dysplasia (RCUD)
2. Refractory Anaemia with ringed sideroblasts
3. Refractory cytopenias with multilineage dysplasia (RMCD)
4. Refractory Anaemia with excess blasts type-1 (RAEB-1)
5. Refractory Anaemia with excess blasts type-2 (RAEB-2)
6. MDS associated with isolated del(5q)
7. Childhood MDS, including refractory cytopenia of childhood
8. MDS unclassifiable (MDS-U)

ETIOLOGY AND PATHOPHYSIOLOGY

MDS is a disease of aging suggesting random cumulative intrinsic and environmental damage to marrow cells. It is associated with exposure to radiation, benzene,as a late toxicity of cancer treatment usually a combination of radiation and radiomimetic alkalyting agents like busulphan, nitrosourea, procarbazine or DNA topoisomerase inhibitors. Acquired aplastic anaemias, Fanconi anaemia and constitutional marrow failure diseases can evolve into MDS. However, typical MDS doesnot seem to have environmental exposures or previous hematological illnesses.

Pathophysiology has been linked to mutations and chromosome abnormalities in some specific MDS syndromes. The 5q- deletion leads to heterozygous loss of ribosomal protein gene that is also mutant in Diamond-Blackfan anaemia, and both are characterised by deficient erythropoiesis. An immune pathophysiology may underlie trisomy 8 MDS but the mechanism is not clearly understood.

CLINICAL FEATURES

Most symptoms are that of anaemia and patients complains of gradual onset of fatigue and weakness, dyspnea. About one-half of patients are asymptomatic and are discovered incidentally on routine blood tests. Fever and weight loss are unusual. History should stress on previous chemotherapy and radiation exposure. Physical examination is remarkable for signs of anaemia. Approximately 20% have splenomegaly. Some unusual skin lesion including sweet syndrome occur with MDS. In younger children stereotypical anomalies point to a constitutional syndrome. Prognosis strongly correlates with the proportion of marrow blasts.

LABORATORY STUDIES

BLOOD:

Anaemia is present in most cases. Isolated neutropenia and thrombocytopenia is unusual. Macrocytosis is common, but the smear maybe dimorphic. Platelets are also large and lack granules. Neutrophils are

hypogranulated with hyposegmented, ringed, or contain abnormally segmented nuclei; Dohle bodies. Myeloblasts correlates with marrow myeloblasts.

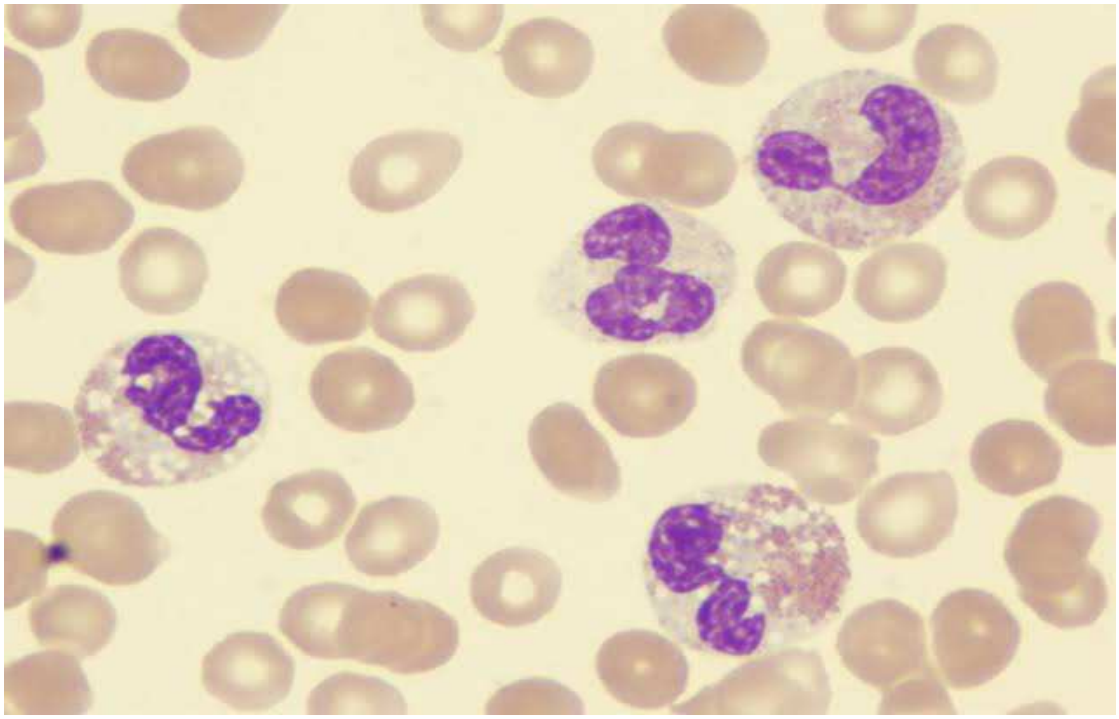


Figure: Peripheral smear of MDS showing hypogranulated eosinophils with Pseudo Pelger huet cells (hypolobulated nucleus)

BONE MARROW:

Is usually normal or hypercellular but in ~20% is hypocellular. No characteristic marrow feature distinguishes MDS but dyserythropoietic changes and ringed sideroblasts;hypogranulated and hyposegmented granulocytes, increased myeloblasts;reduced number or disorganised nuclei of megakaryocytes are commonly observed. Cytogenetics and fluorescent in situ hybridisation (FISH) can identify chromosomal abnormalities.

TREATMENT:

Only hematopoietic stem cell transplantation offers cure of MDS. Two epigenetic modifiers, Azacitidine and Decitabine have shown to improve survival. ATG, cyclosporine and alemtuzumab are effective in younger patients. Supportive care plays an important role.

HIV AND THE HEMATOPOIETIC SYSTEM

Disorders of the hematopoietic system including lymphadenopathy, anaemia, leucopenia, and/or thrombocytopenia are common throughout the course of HIV infection and may be the direct result of HIV, manifestations of secondary infections and neoplasms, or side effects of therapy.[41,42] Direct histologic examination and culture of lymph node or bone marrow tissue are often diagnostic. A significant percentage of bone marrow aspirates from patients with HIV infection have been reported to contain lymphoid aggregates, the precise significance of which is unknown. Initiation of HAART lead to reversal of most hematologic complications that are the direct result of HIV infection[43,44].

CAUSES OF BONE MARROW SUPPRESSION IN PATIENTS WITH HIV INFECTION

- HIV infection
- Mycobacterial infections
- Fungal infections

- B19 parvovirus infection
- Lymphoma
- Medications
    - Zidovudine
    - Dapsone
    - Trimethoprim/sulfamethoxazole
    - Pyrimethamine
    - 5-Flucytosine
    - Ganciclovir
    - Interferon-gamma
    - Trimetrexate
    - Foscarnet.

SYSTEMIC LUPUS ERYTHEMATOSUS

In patients with SLE apart from antibodies to double strand DNA and anti-smith antibodies, antibodies that target each of the cellular blood elements are also common; Antierythrocyte and Antiplatelet antibodies against erythrocyte membrane and surface and altered cytoplasmic antigens on platelets respectively. Antibodies that bind to lymphocytes and neutrophils have been described. Anaemia is present in about one-half of patients and is multifactorial. It can be associated with a positive Coombs test or microangiopathic hemolysis or reflect chronic disease (normochromic, normocytic). Leucopenia, particularly lymphopenia, is observed, with the

lymphocyte count inversely proportional to the disease activity. An increased tendency for lymphocytes to undergo spontaneous apoptosis may contribute to lymphopenia. Idiopathic thrombocytopenic purpura can be an early manifestation of SLE, and thrombocytopenia can sometimes lead to a life threatening haemorrhage[45,46].

MALARIA

It is a parasitic infection caused by obligate intracellular protozoa of the genus Plasmodium[47].Anaemia is the most prominent hematological manifestation of malarial infection and is most marked with the species, *plasmodium falciparum*, which invades erythrocytes of all ages. Cellular disruption and hemoglobin digestion lead directly to hemolysis**.** An inadequate bone marrow response to anaemia is seen, with relative reticulocytopenia. Leucocyte number may be slightly increased or normal; however, leucopenia as a result of splenomegaly and impaired marrow function is characteristic. Thrombocytopenia is seen in nearly 70% of cases[48]. The effect on the hematopoietic system of plasmodium falciparum is similar to that of plasmodium vivax not only in the red cell lineage but also in other cell lines, characterized by dyserythropoiesis and ineffective erythropoiesis[49].

DENGUE INFECTION

The hemophagocytic syndrome is an atypical and rare manifestation of dengue fever. In the present era, dengue viral infection is leading organism responsible for secondary hemophagocytic lymphohistiocytosis (HLH) in tropical countries[50,51]

It has also been described with various infections, malignancy and auto-immune disorders. HLH is a hyperinflammatory condition which is caused by hypercytokinemia due to excessively stimulated but ineffective immune response. There is overstimulation of macrophages or monocytes that leads to overproduction of various pro-inflammatory cytokines IFN-gamma, TNF-alpha, IL-6,IL-10 and the macrophage colony stimulating factor. These activated cells engulf the red blood cells, white blood cells and thrombocytes leading to cytopenia.

Acquired aplastic anaemia as a result of immune dysregulation triggered by dengue virus is one proposed mechanism and there are only few reported cases in the literature. The immune response is dominated by oligoclonal expanded cytotoxic T calls that targets hematopoietic stem and progenitor cells, inducing their cell death via apoptosis and hematopoietic failure[52]. Other viruses like Parvovirus B19 and hepatitis also shares the same mechanism. The other mechanism in which dengue virus infection causes aplastic anaemia is the replication of the virus in the hematopoietic cells, which directly damages these hematopoietic cells peripherally or in the bone marrow[53].

MATERIALS AND METHODS

This study was done at Rajiv Gandhi Government General Hospital, Chennai for a period of Six months from August 2017 to January 2018. The study was performed after procuring informed written consent from all the participants involved. Clearance was obtained from the Ethical Committee of Madras Medical College & RGGGH, Chennai.

STUDY DESIGN

The study design is a cross sectional study.

POPULATION

The study population included 100 persons who met the criteria for Pancytopenia admitted in the Institute of Internal Medicine, Ragiv Gandhi Government General Hospital.

INCLUSION CRITERIA

1. Age >15years
2. Anaemia as defined by WHO
    a) <13g/dl in males
    b) <12g/dl in females
3. Leucopenia [TLC <4000/dl]
4. Thrombocytopenia [Platelet count <1,50,000]

EXCLUSION CRITERIA

1. Patients who have received or are receiving cancer chemotherapy.
2. Patients who have received or are receiving cancer Radiotherapy.
3. Patients who received blood transfusion.
4. Not given consent for the study.

METHODOLOGY

After obtaining clearance and approval from the institutional ethics committee and written informed consent from the patients admitted to RGGGH with pancytopenia who have met both the inclusion and exclusion criteria, they were subjected to detailed history taking including the presenting complaints, fever, bleeding manifestations, dietary history, alcohol, smoking or other addictions and meticulous physical examination including pallor, icterus, hepatomegaly, splenomegaly, lymphadenopathy and bony tenderness. Blood samples were collected for complete blood counts including hemoglobin, total leucocyte count, platelete count and various parameters such as PCV, MCV, MCH, MCHC, peripheral smear examination and LFT. Also Viral markers such as HBsAg and Anti-HCV and HIV serology, ultrasound abdomen and Chest Xray was done for all patients. Patients with history of fever were subjected to fever profile including peripheral smear for Mp,Mf, dengue and MSAT test. Vitamin B12 and Folate assay, upper GI endoscopy, thyroid function test, ANA profile was done whenever required. Bone marrow study was done for selected number of patients when the diagnosis was in doubt.

STATISTICAL ANALYSIS: Data analysis was done with using the statistical analysis SPSS, version 13 software.

FINANCIAL SUPPORT **:** Nil

CONFLICTS OF INTEREST : None

OBSERVATIONS AND RESULTS

DEMOGRAPHICS

TABLE 1.1: Distribution of pancytopenia according to sex.

Sex	Frequency
Males	57
Females	43
TOTAL	100

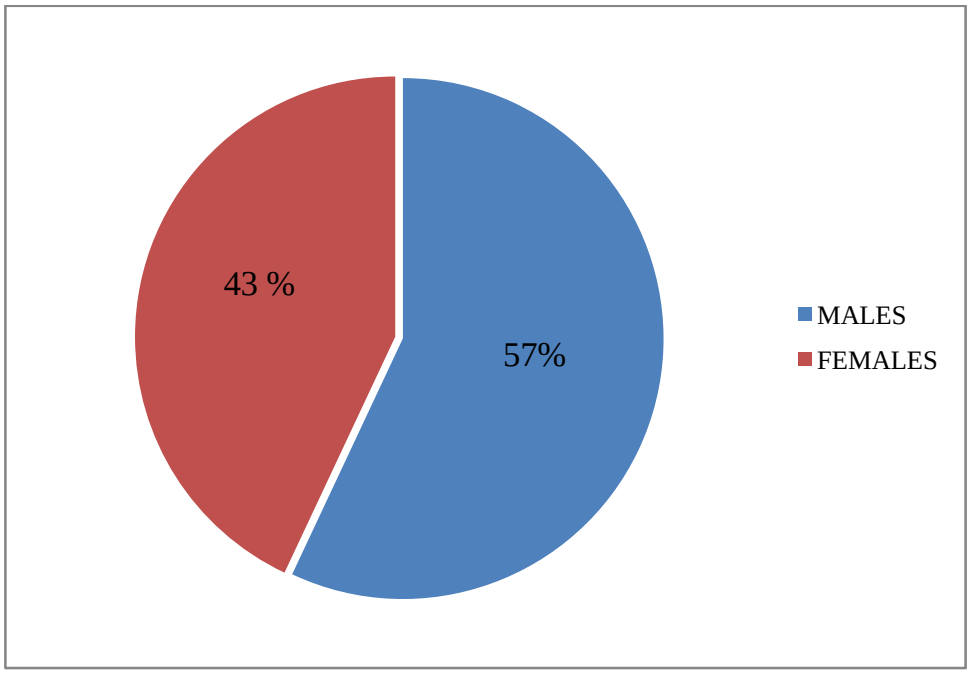


Figure 1.1: Distribution of pancytopenia according to sex

In our study, out of 100 patients 57% were males and 43% were females.

TABLE 1.2: Age & sex wise distribution of pancytopenia.

Age	Male	Female	Total
<20	8	3	11
21-30	10	8	18
31-40	15	10	25
41-50	13	8	21
>50	11	14	25
TOTAL	57	43	**100**

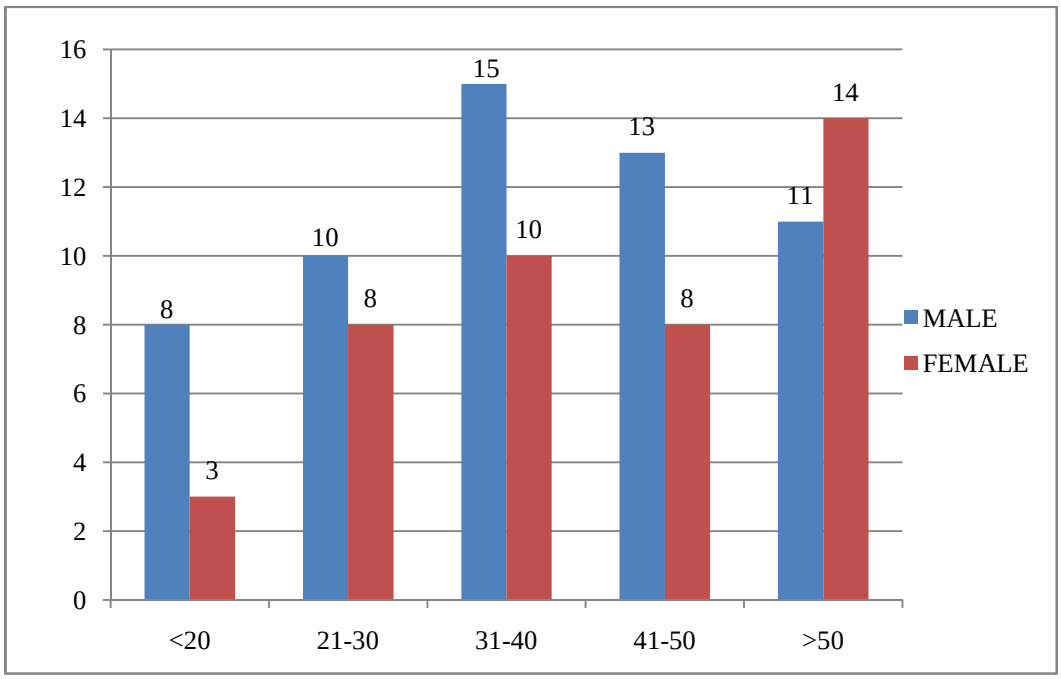


Figure 1.2 : Distribution of pancytopenia according to age & sex.

The mean age of patients presented with pancytopenia in our study was 40 years with a standard deviation of 14 years.

Mean age for males were 38.4 years and that for females were 42.3 years.

Maximum number of cases was seen in age group of 31-40 years & > 50 years with a combined percentage of 50.

Amongst males, the maximum number of cases were in age group of 31-40 years with p-value 0.55 which is not statistically significant.

Amongst females the maximum number of cases were in age group of >50 years with p-value of 0.55 which is also not statistically significant.

CLINICAL FEATURES

SYMPTOMS AT PRESENTATION

TABLE 2.1: Frequency of symptoms associated with pancytopenia.

S.no	Symptoms	Frequency
1.	Easy fatiguability	91
2.	Fever	57
3.	Bleeding tendency	37
4.	Bone pain	6
5.	Night sweats	7
6.	Weight loss	32
7.	Anorexia	60
8.	Dyspnea	52

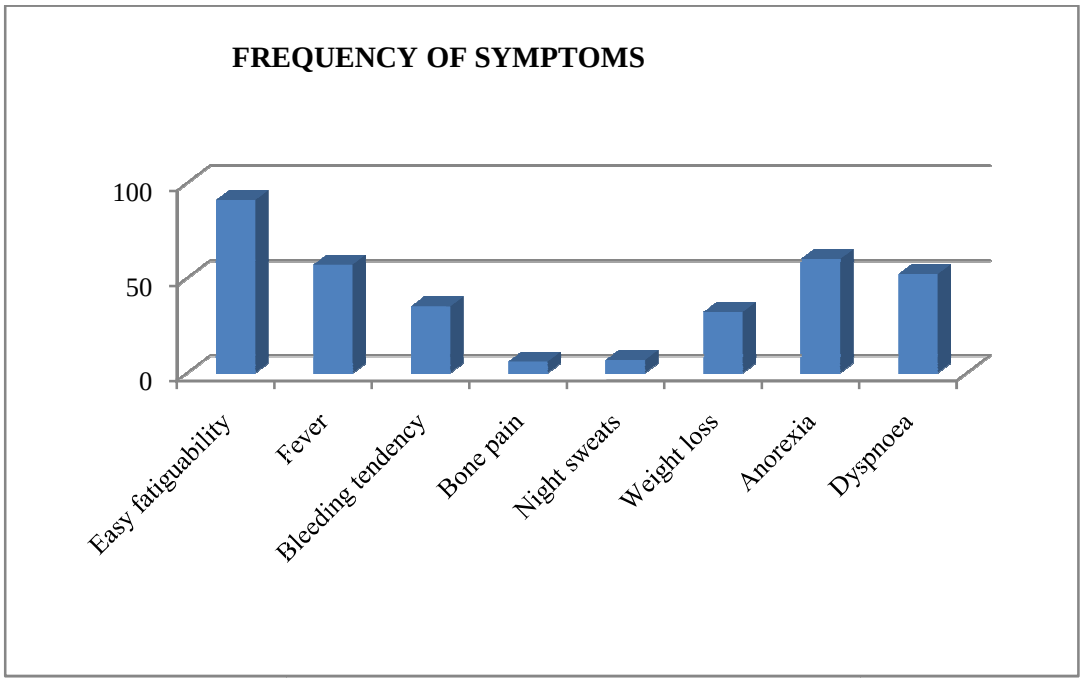


Figure 2.1: Bar diagram showing frequency of symptoms of pancytopenia.

Symptoms of anemia such as easy fatigueability and dyspnea was seen in 91% and 52% of patients respectively.

Fever was present in more than half of the patients at presentation.

Bleeding manifestation was present in 35% of patients.

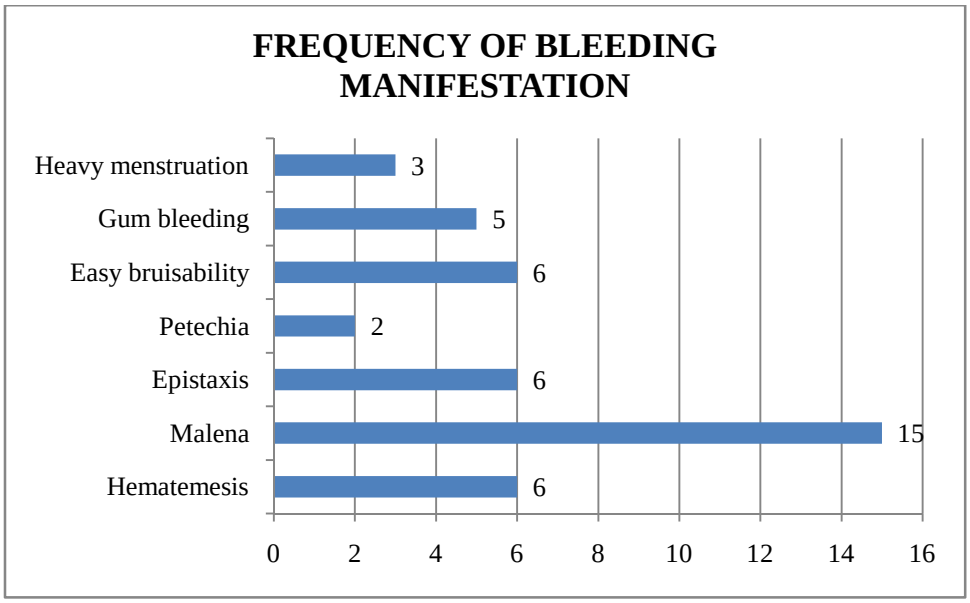


Figure 2.2: Frequency of various bleeding manifestation.

Malena was the major bleeding manifestation in our study and was present in 15 patients and most of the cases had esophageal varices.

PHYSICAL EXAMINATION

TABLE 2.2: Physical examination findings of pancytopenia patients.

S.no	Clinical findings	Frequency
1.	Palor	97
2.	Icterus	11
3.	Hepatomegaly	15
4.	Splenomegaly	27
5.	Lymphadenopathy	3
6.	Sternal tenderness	5
7.	Gum hypertrophy	2

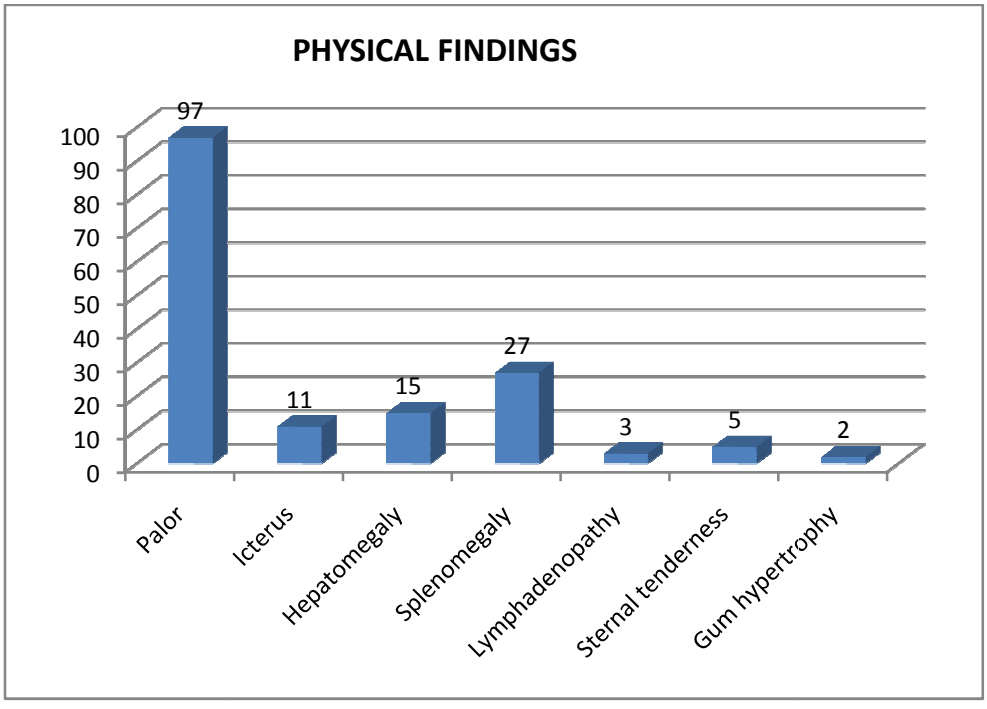


Figure 2.3 : Bar diagram showing physical examination findings.

Pallor was seen in 97% of patients and it correlated well with anaemia symptoms at presentation.

Icterus was seen in 11% of patients and most of them had chronic liver disease.

27% of patients had splenomegaly and was seen in all cases of hypersplenism and ALL. Some cases of megaloblastic anaemia(21%) and MDS(25%) also had splenomegaly.

Hepatomegaly was present in 15% of patients with pancytopenia and majority of them had megaloblastic anaemia and acute leukemia.

Lymphadenopathy was found in 3% of patients and all the patients had acute leukemia.

Sternal tenderness 5% and gum hypertrophy 2% were exclusively found in acute leukemia.

INVESTIGATIONS

TABLE 3.1 : Hematologic parameters in pancytopenia.

S.no	Investigation		Frequency
1.	Hb	<5	40
		5-8	34
		>8	26

S.no	Investigation		Frequency
2.	TLC	<1000	5
		1001-2500	38
		>2500	57

S.no	Investigation		Frequency
3.	Platelets	<50000	55
		50001-80000	22
		>80000	23

S.no	Investigation		Frequency
4.	Reticulocyte count	<0.5	25
		0.6-1	32
		>1	43

Hemoglobin percentage:

40% of patients had haemoglobin <5g/dl, 34% in the range 5-8g/dl and 26% of patients had >8g/dl.

Total leucocyte count:

More than half of the patients 57% had TLC of 2500-3900 cells/mm^3, 38% of the cases were in the range of 1001-2500 cells/mm^3 and 5% of the cases had <1000 cells/mm^3

Platelets:

More than half of the patients had platelet count of <50000 cells/mm^3, 22% of the cases were in the range of 50001-80000 cells/mm^3 and 23% had >80000 cells/mm^3

Reticulocyte count:

25% of the patients had reticulocye count of <0.5, 32% of the patients had their reticulocyte count in the range of 0.6-1 and most of the cases had their reticulocyte count >1 (43%).

T-TEST FOR HEMATOLOGICAL PARAMETERS AND CLINICAL PRESENTATION

a. TLC count and occurrence of fever 0.055 (not significant)
b. Platelet count and occurrence of bleeding manifestation 0.88 (Not significant)

c. Hemoglobin count and occurrence of easy fatigueability 0.8 (not significant) or dyspnea 0.73 (Not significant)

TABLE 3.2 : Peripheral smear study

S.no	Peripheral smear findings	Frequency
1.	MCHA	48
2.	NCNC	24
3.	Macrocytes	29
4.	Anisopoikilocytosis	39
5.	Lymphocytosis	9
6.	Immature blast	5
7.	Hypersegmented neutrophils	26
8.	Erythroblast	7
9.	Leucopenia	42
10.	TCP	69

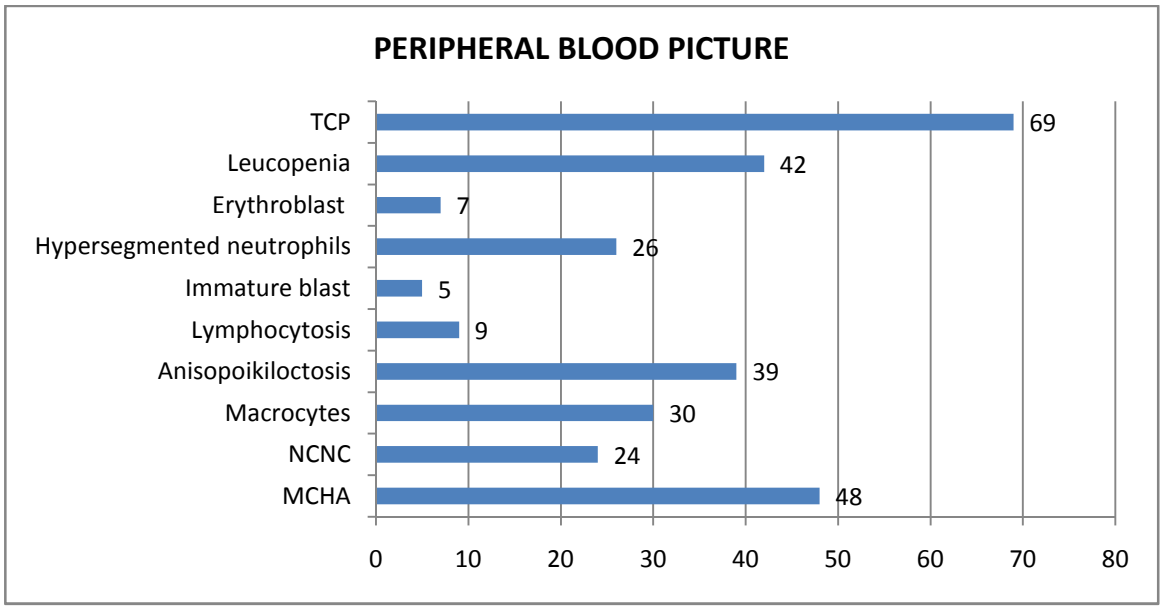


Figure 3.1 : Bar diagram of peripheral smear findings.TCP-thrombocytopenia, NCNC-normocytic normochromic anaemia,MCHA-microcytic hypochromic anaemia

More than half of the patients had thrombocytopenia (69%) and were present in clumps.

Majority of the patients had microcytic hypochromic anaemia (48%) and anisopoikilocytosis (39%). Macrocytes was present in 30% and hypersegmented neutrophils in 26% of patients and almost all of them had megaloblastic anaemia. Rest of the patients had normocytic norchromic anaemia in 24%.

Leucopenia was present in 42% of patients. Immature blasts in 5% of patients and exclusively found in leukemia patients. Lymphocytosis was found in 9% of patients and most of them had dengue positive or other viral infection.

VARIOUS ETIOLOGIES OF PANCYTOPENIA AND THEIR DISTRIBUTION

TABLE 4.1 : Etiology of pancytopenia.

Sl. No	Etiology	Frequency
1.	Megaloblastic Anaemia	37
2.	Aplastic Anaemia	24
3.	Hypersplenism	13
4.	MDS	6
5.	CTD	3
6.	Dengue	4
7.	Malaria	4
8.	ALL	2
9.	AML	3
10.	HIV	1
11.	Disseminated TB	1
12.	Viral Induced	2
	TOTAL	100

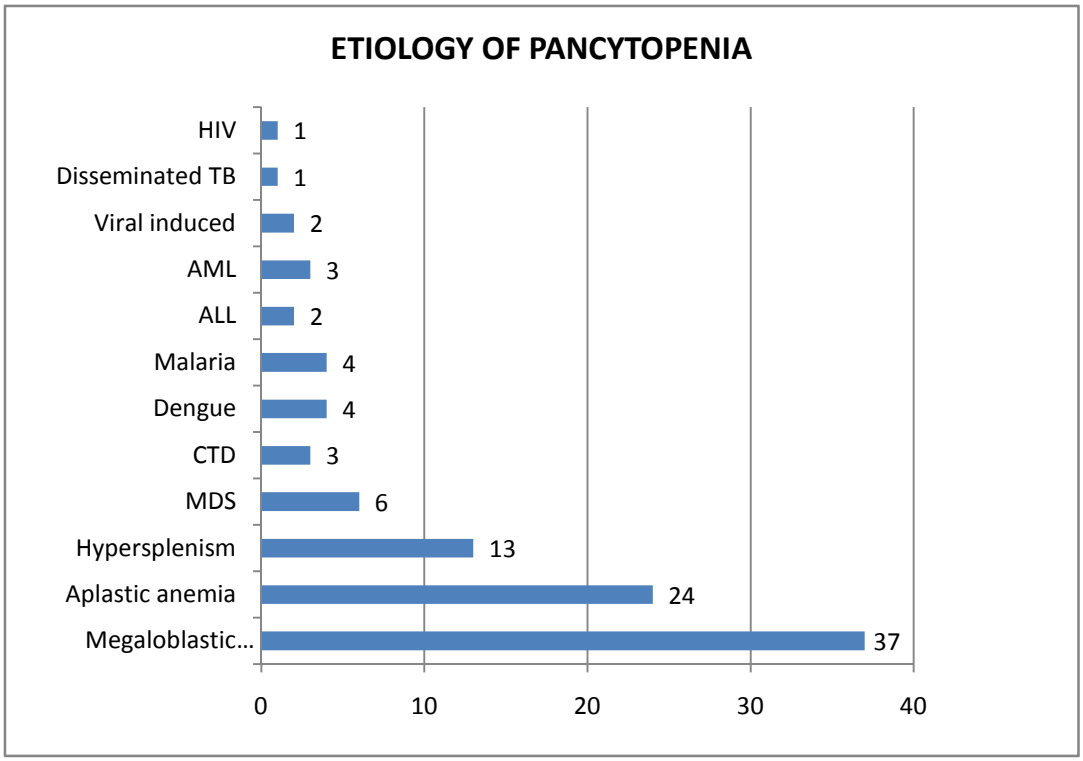


Figure 4.1 : Bar chart showing various etiologies of Pancytopenia.

More than half of the cases (61%) was diagnosed to have either megaloblastic anaemia or aplastic anaemia.

Megaloblastic anaemia was found to be the most common cause of pancytopenia and was found in 37% of patients. The second most common cause was aplastic anaemia and was found in 24% of patients.

Hypersplenism was diagnosed in 13% of patients and MDS in 6%. The other etiologies of pancytopenia were MDS (6%), connective tissue disorders such as SLE (3%), infections such as dengue(4%), malaria(4%), disseminated TB(1%), HIV(1%) and other viral induced(2%).

Acute leukemias were diagnosed in 5% of patients(ALL & AML).

TABLE 4.2: Age wise distribution of various etiology of pancytopenia.

Age / **Diagnosis**	**<20**	**21-30**	**31-40**	**41-50**	**>50**
Megaloblastic anaemia	3	5	12	11	6
Aplastic anaemia	5	3	3	2	11
Hypersplenism	0	2	4	6	1
MDS	0	1	0	0	5
CTD	0	2	1	0	0
Dengue	0	2	2	0	0
Malaria	1	1	1	1	0
ALL	1	0	0	1	0
AML	1	0	1	1	0
Disseminated TB	0	0	1	0	0
Viral induced	0	2	0	0	0
HIV	0	0	0	0	1
TOTAL	11	18	25	21	25

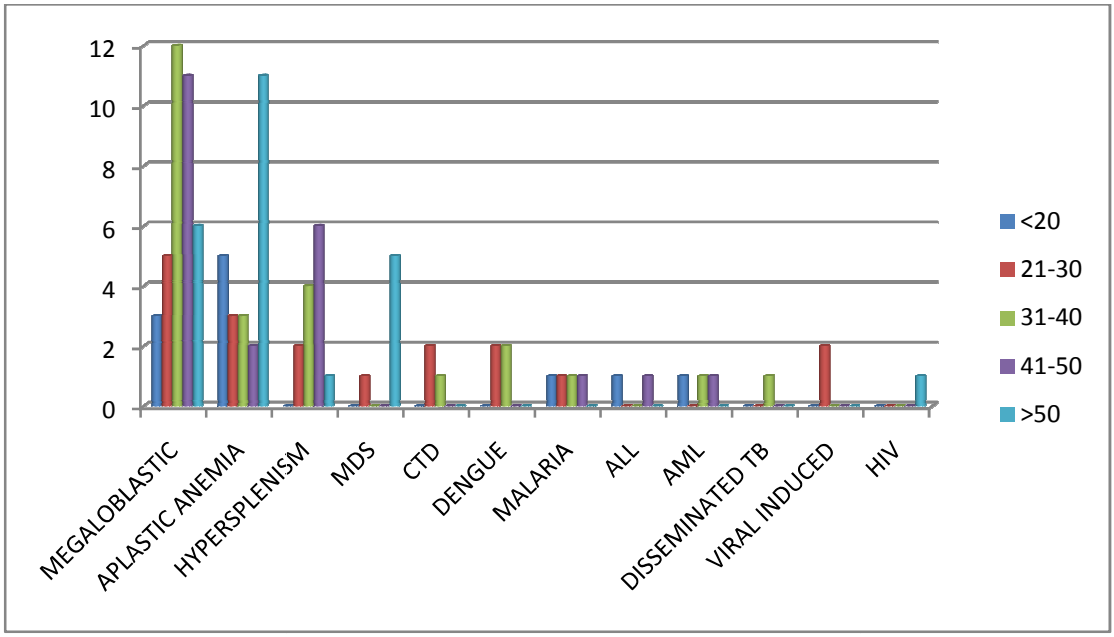


Figure 4.2: Bar chart showing the age-wise distribution on various etiologies of Pancytopenia. ALL-acute lymphoblastic leukemia, AML-acute myeloid leukemia, CTD- connective tissue disorder, MDS-myelodysplastic syndrome, HIV-human immunodeficiency Virus, TB-tuberculosis.

Overall, the pancytopenia cases was found to be more common in age group of 31-40 years and >50years age group with a combined percentage of 50%.

Most common etiology in various age groups:

In age group <20 years, aplastic anaemia was found to be more common 45.4%.

Age group 21-30 years, megaloblastic anaemia (27.7%) followed by aplastic anaemia (16.6%) were more common.

Age group 31-40 years, megaloblastic anaemia was found to be more common (48%).

Age group 41-50 years, megaloblastic anaemia was again found to be more common (52%).

Age group > 50 years, aplastic anaemia was found to be more common (44%).

TABLE 4.3: Sex wise distribution of pancytopenia on various etiologies.

DIAGNOSIS	MALE	FEMALE	M:F
Megaloblastic anaemia	21	16	1.3:1
Aplastic anaemia	13	11	1.2:1
Hypersplenism	8	5	1.6:1
MDS	4	2	2:1
CTD	1	2	0.5:1
Dengue	2	2	1:1
Malaria	3	1	3:1
ALL	1	1	1:1
AML	1	2	0.5:1
Viral induced	1	1	1:1
Disseminated TB	1	0	
HIV	1	0	
TOTAL	57	43	**1.3:1**

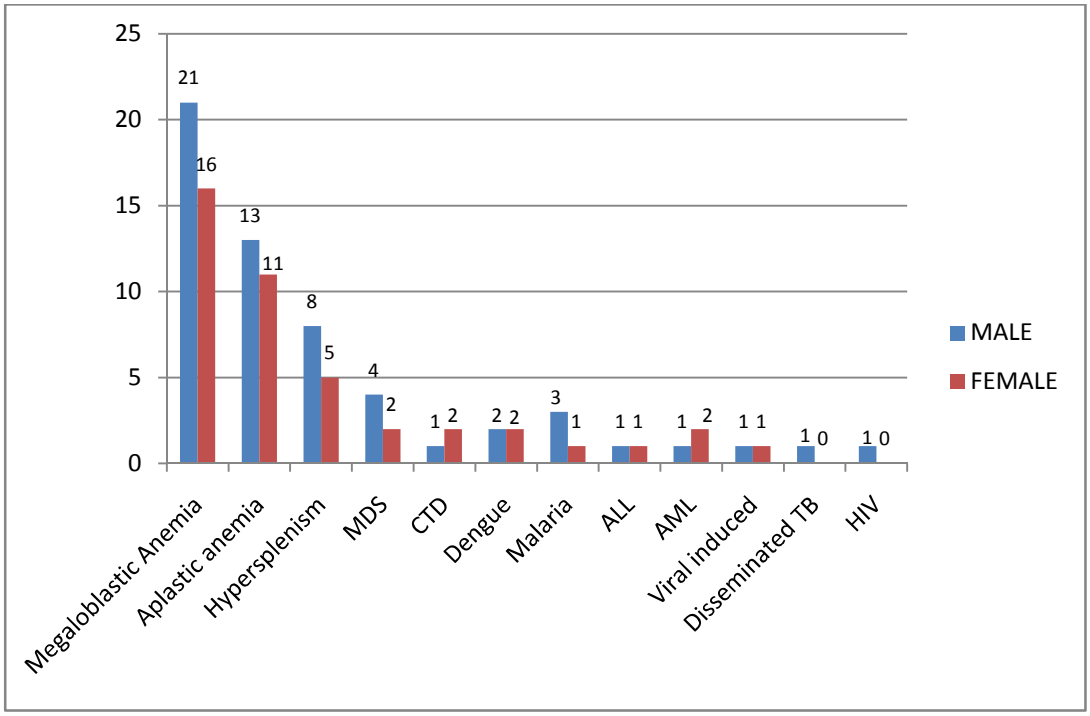


Figure 4.3: Bar chart showing Sex wise distribution on various etiology of pancytopenia.

In Myelodysplastic syndrome and Connective tissue disorder, females were found to be more common with a male:female ratio of 0.5:1.

While megaloblastic anaemia, aplastic anaemia and hypersplenism were more common in males.

IMAGING

Ultrasound abdomen was done for all patients.

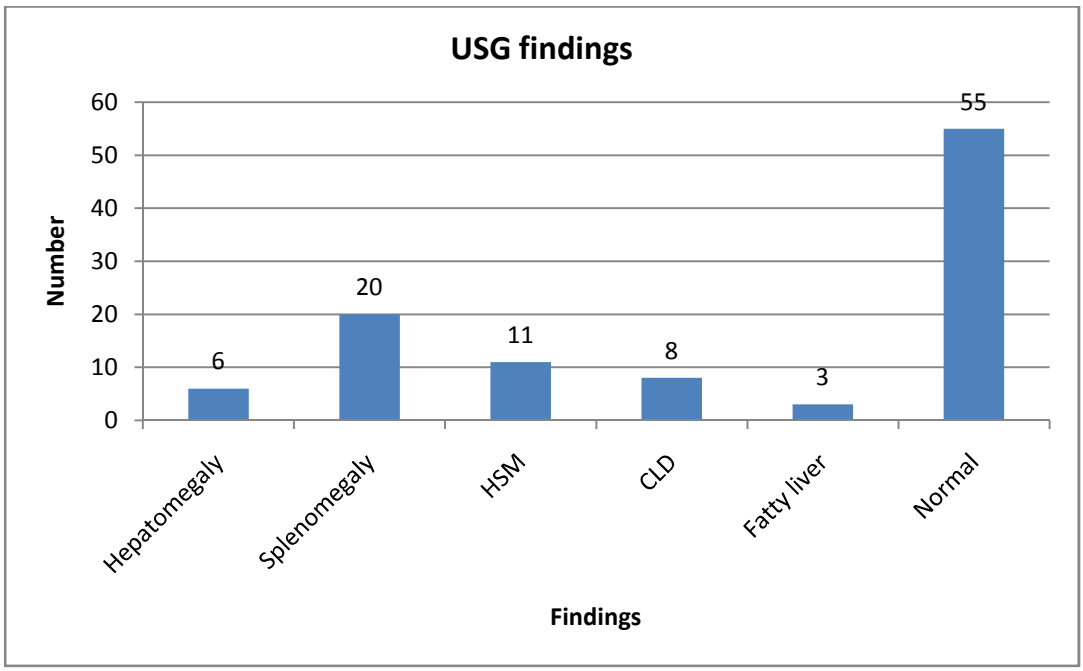


Figure 4.4 : Figure showing USG findings.CLD-chronic liver disease, HSM- hepatosplenomegaly, USG- ultrasound.

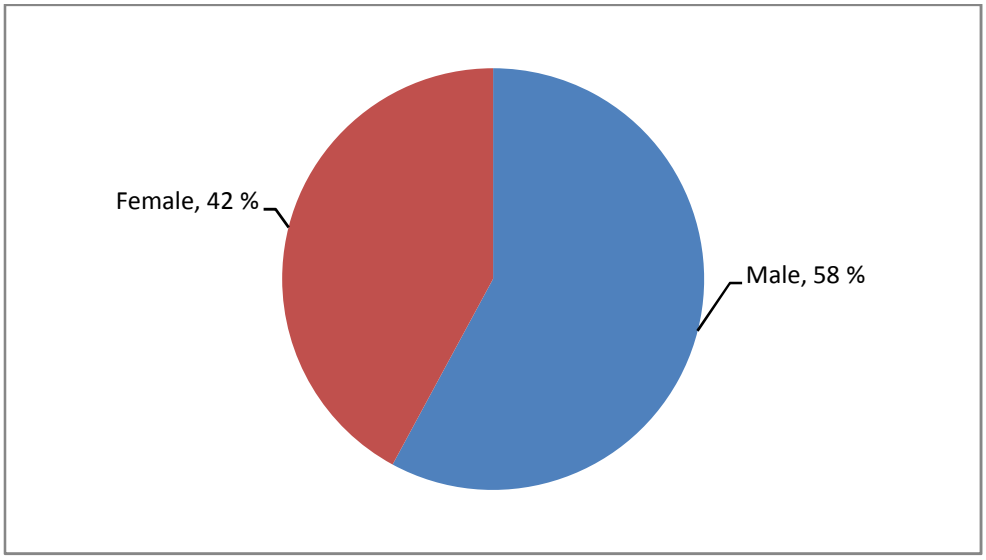
Splenomegaly alone was the most common finding(20) and most of the patients had megaloblastic anaemia, hypersplenism or acute leukemia. Hepatosplenomegaly was found in 11 patients, CLD in 8 patients and Fatty liver was seen in 3 patients, in the latter three, all the patients were found to be alcoholic.

MEGALOBLASTIC ANAEMIA

Megaloblastic anaemia was found to be the most common etiology for pancytopenia in our study and was found in 37% of cases with a slight male preponderance in the ratio of 1.3:1.

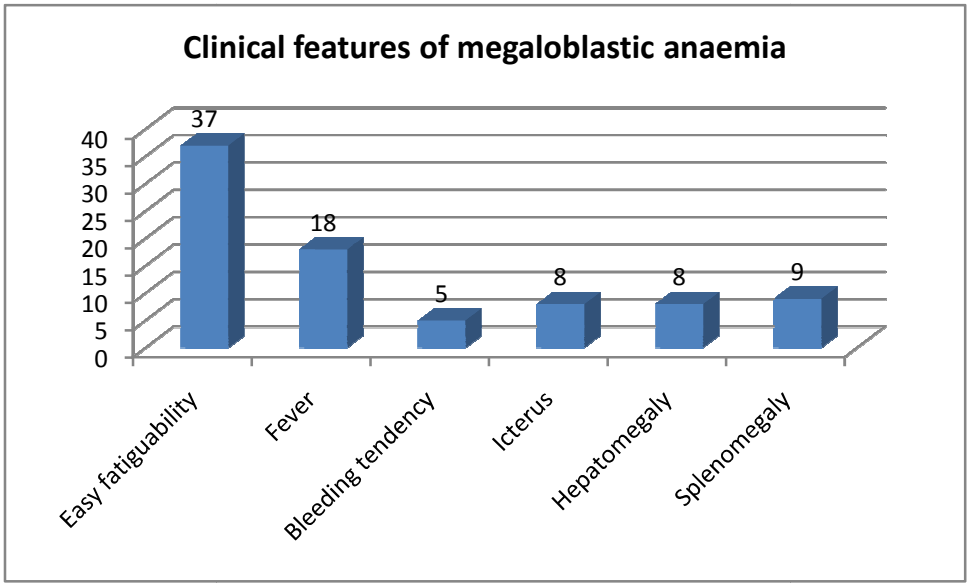
The mean age for megaloblastic anaemia was 39.8 years with a range of 17-60 years.

FIGURE 5.1 : Pie-chart showing sex-wise distribution of patients.



Of the 37 megaloblastic anaemia in our study, 58% of cases were males and 42% were females.

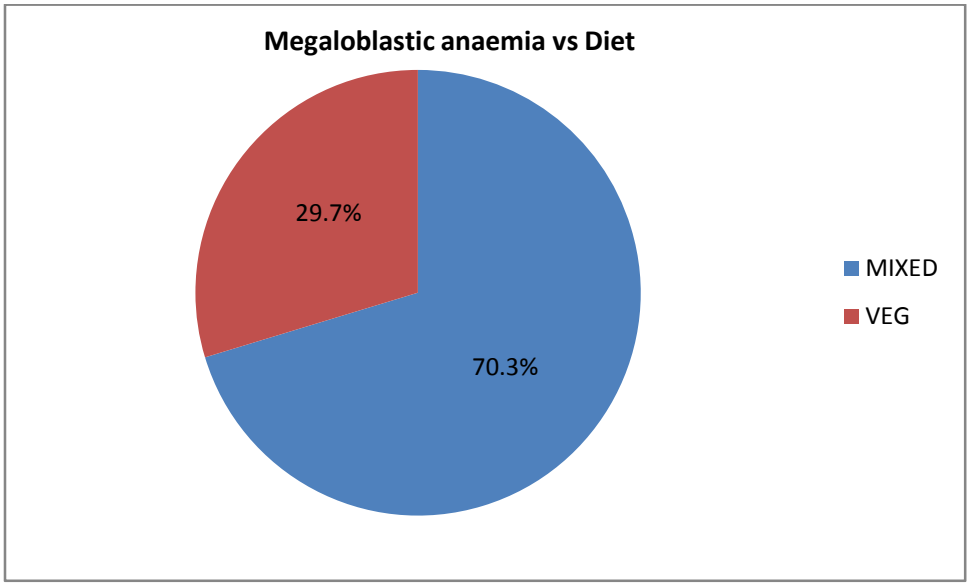
FIGURE 5.2 : Bar chart showing various clinical features.



Almost all patients of megaloblastic anaemia presented with easy fatigueability (100%). Fever was the next common presenting complaint (48.6%) and 13.5% of these patients had some bleeding manifestation.

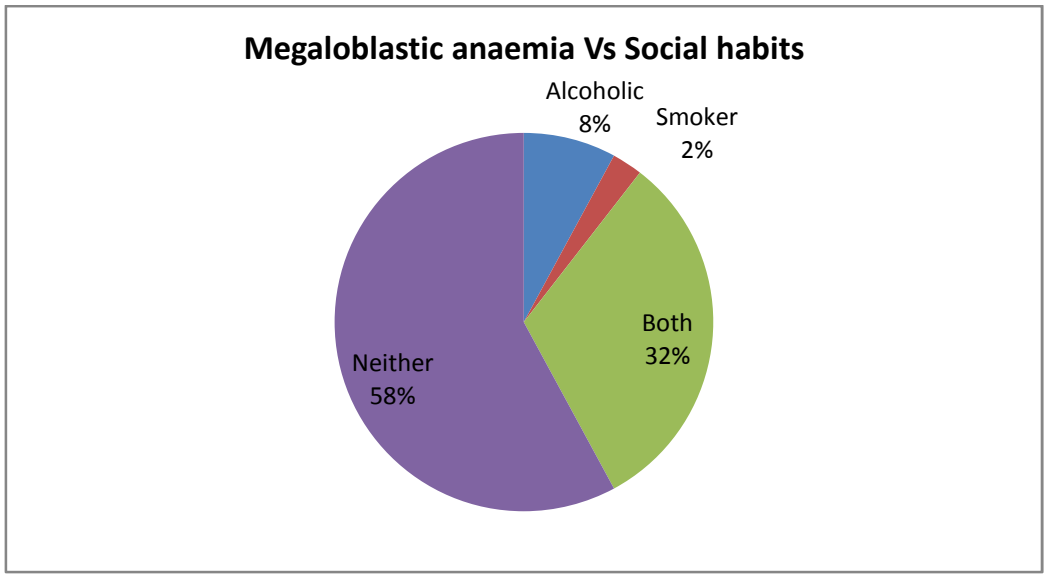
On examination, splenomegaly was present in 9 patients (24.3%) and hepatomegaly was present in 8 patients (21.6%)

FIGURE 5.3: Pie-chart showing frequency of megaloblastic anaemia with dietary habits.



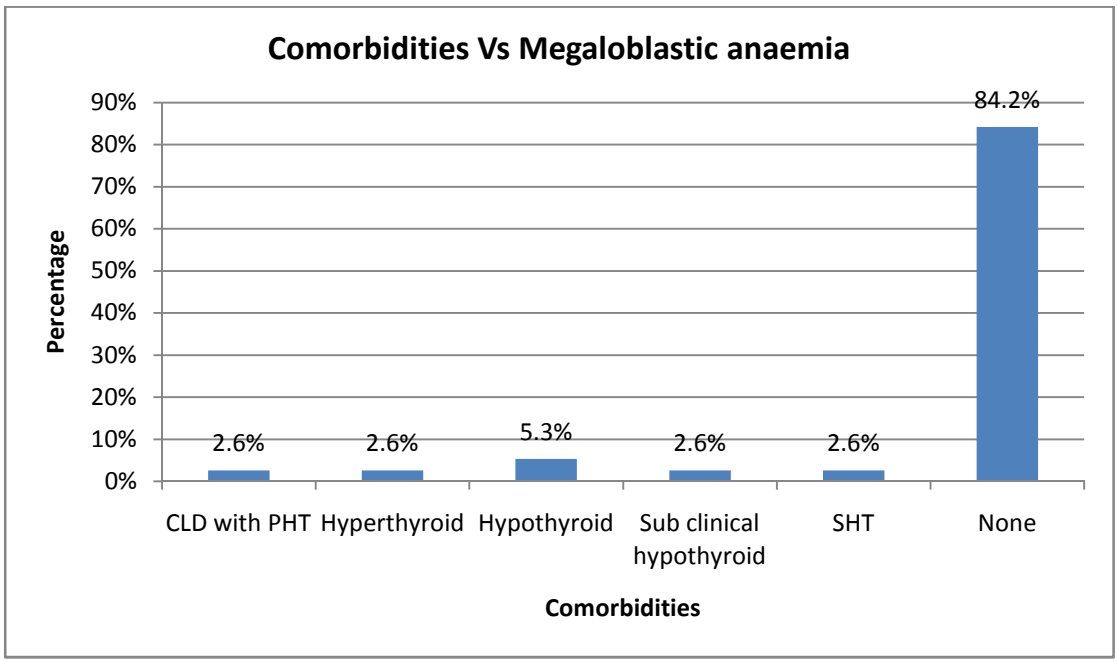
29.7% of the patients with megaloblastic anaemia were found to consume pure vegetarian diet.

FIGURE 5.4: Pie-chart depicting the relationship of alcohol and smoking with megaloblastic anaemia.



42% of megaloblastic anaemia cases were either alcoholic or smoker or both.

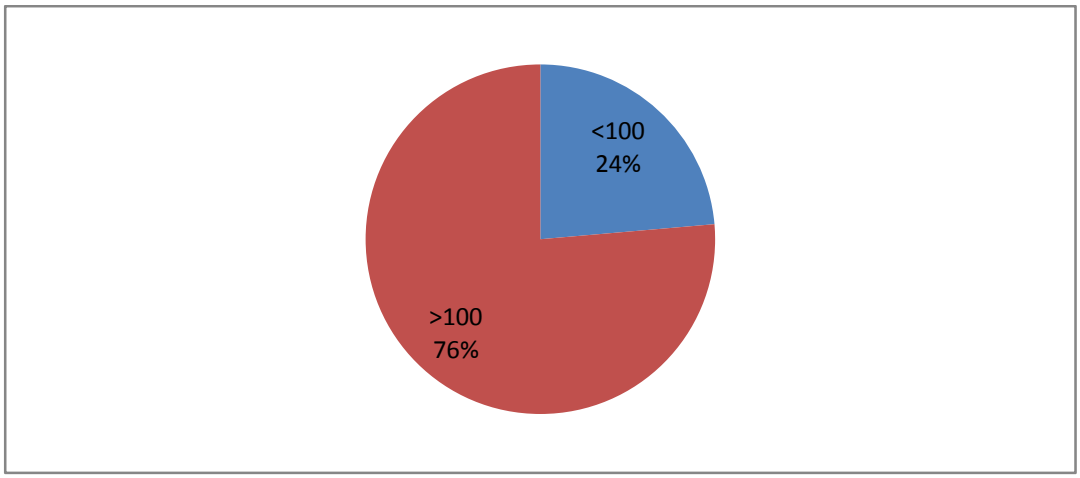
FIGURE 5.5 : Bar diagram showing various co-morbidities and their frequencies.



. CLD-chronic liver disease, PHT-portal hypertension, SHT- systemic hypertension.

Subclinical hypothyroid, hypothyroid, hyperthyroid and CLD were seen in 5 patients which are important cause of megaloblastic anaemia.

FIGURE 5.6 : Pie-chart showing frequency of macrocytosis in patients with megaloblastic anaemia.

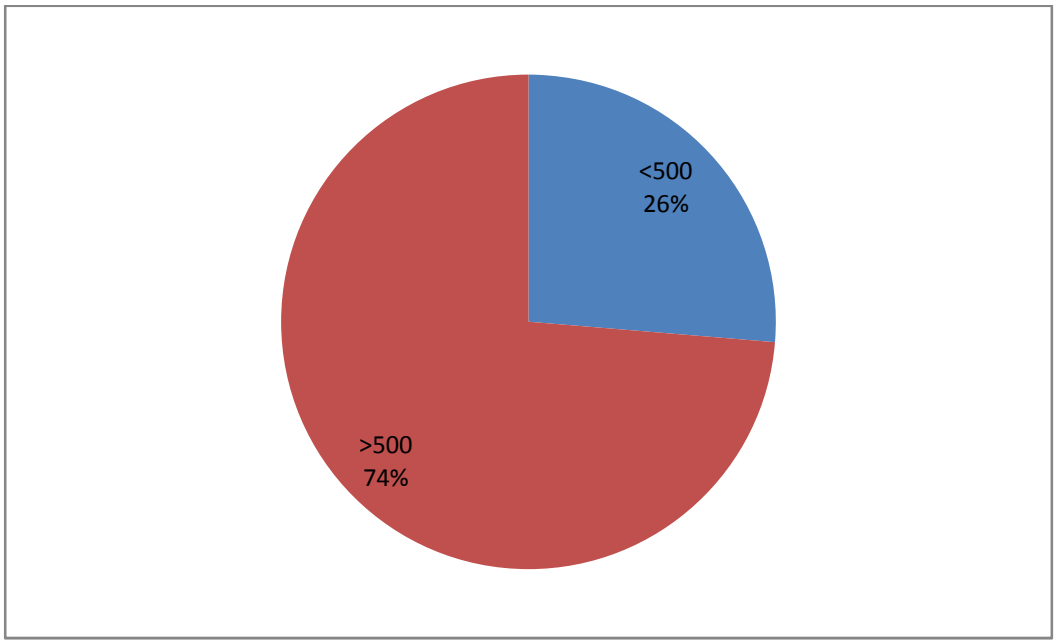


76% of the patients showed macrocytosis in blood picture with MCV>100.

TABLE 5.1: Showing various blood parameters in megaloblastic anaemia.

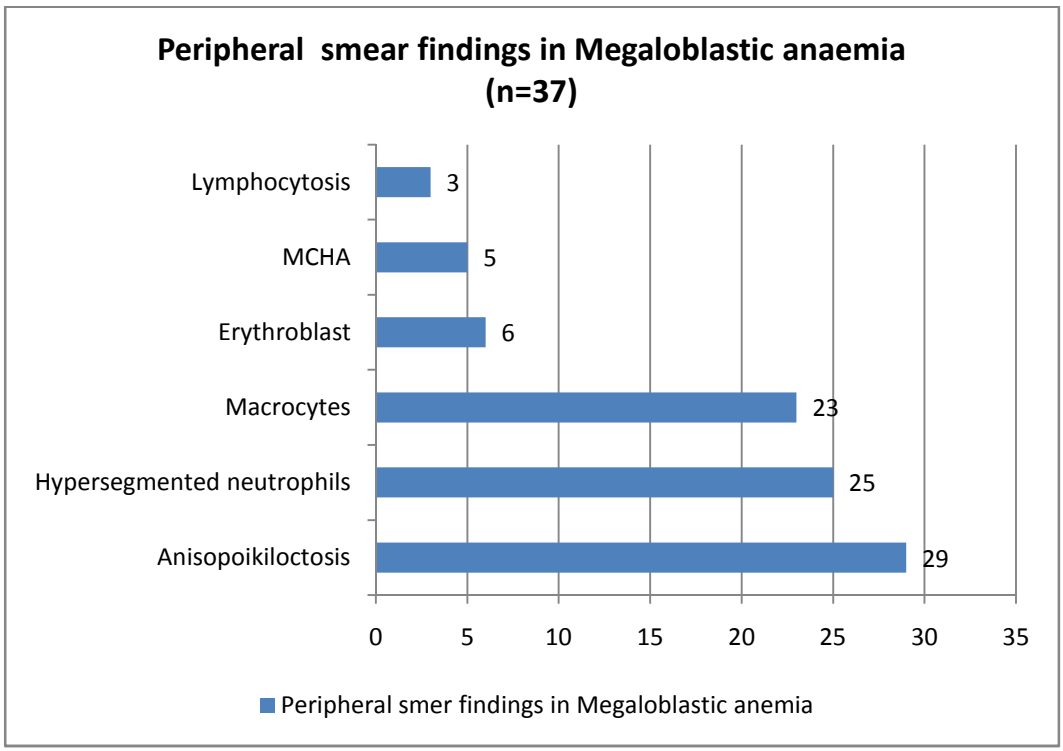
Variable	Hb g/dl	TLC	Platelete
Mean	6.2	2775	2775
Median	5.5	2900	2900
Range	2.8-12	500-3900	500-3900
SD(standard deviation)	2.7	798	798

FIGURE 5.7 : Pie-charting showing the frequency of raised LDH in megaloblastic anaemia.



74% of patients had LDH of >500.

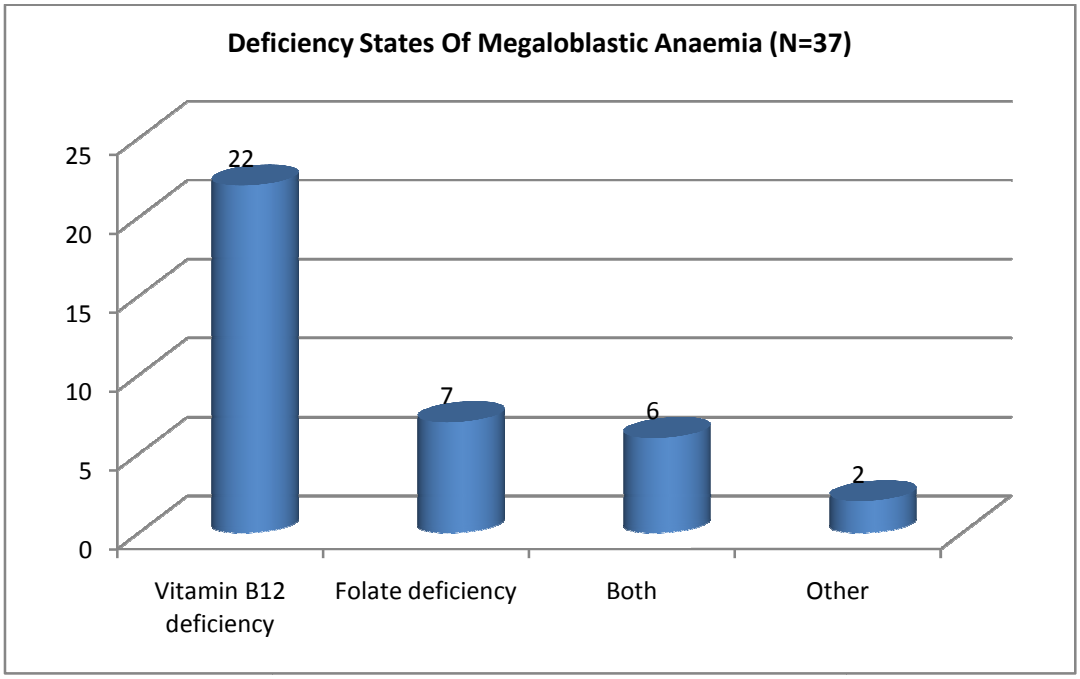
TABLE 5.5: Peripheral smear findings in megaloblastic anaemia.



MCHA – Microcytic Hypochromic Anaemia

Anisopoikilocytosis(78.3%), hypersegmented neutrophils(67.5%) and macrocytes(62.1%) were the predominant peripheral smear finding for megaloblastic anaemia.

FIGURE 5.6 : Etiology of megaloblastic anaemia.



Most of the patients with megaloblastic anaemia had vitamin B12 deficiency alone, 22 out of 37 patients (59.4%). 7 of them had Folate deficiency alone (18.9%) and 6 of them had both Vitamin B12 and folate deficiency (16.2%). In the latter group, most of them were pure vegeterians. Hypothyroidism was seen in 2 patients which was attributable to megaloblastic anaemia.

APLASTIC ANAEMIA

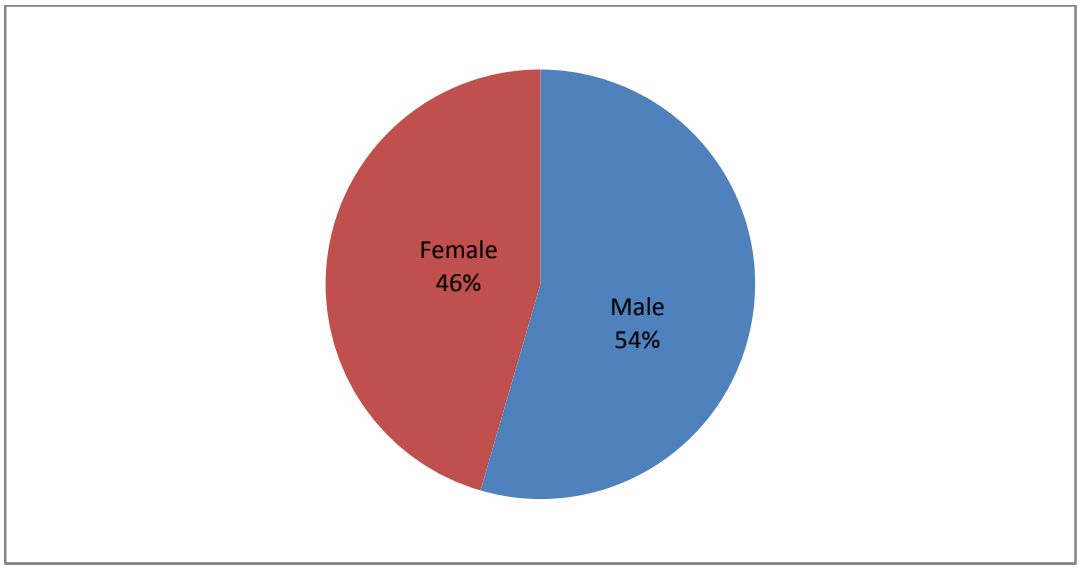
Aplastic anaemia was found to be the second most common cause of pancytopenia in our study (24) with a male to female ratio of 1.1:1.

Fanconi anaemia was diagnosed in 1 female patient and a case of Toulene induced aplasia was diagnosed in 1 male patient.

The overall incidence of aplastic anaemia was predominantly found in two age groups >50 years (45.8%) and <20 years (20.8%).

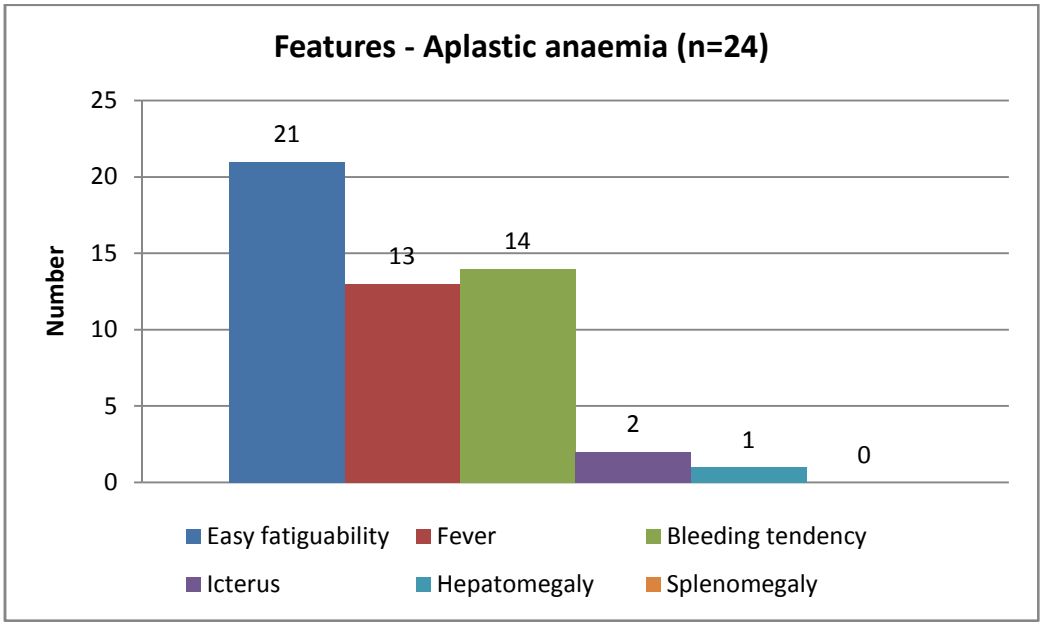
The most common peripheral smear finding of aplastic anaemia was MCHA (91.7%) and leucopenia (79.2%)

FIGURE 6.1: Pie-chart showing sex-wise distribution among patients with aplastic anaemia.



Of the 24 cases, males comprised of 54% and females comprised of 46%.

FIGURE 6.2 : Bar diagram showing clinical features of aplastic anaemia.



Most of them had symptoms of anaemia such as easy fatigueability (87.5%) and dyspnea at presentation. Bleeding manifestation (58.3%) and fever (54.1%) was another major complaints that the patient got admitted with.

HYPERSPLENISM

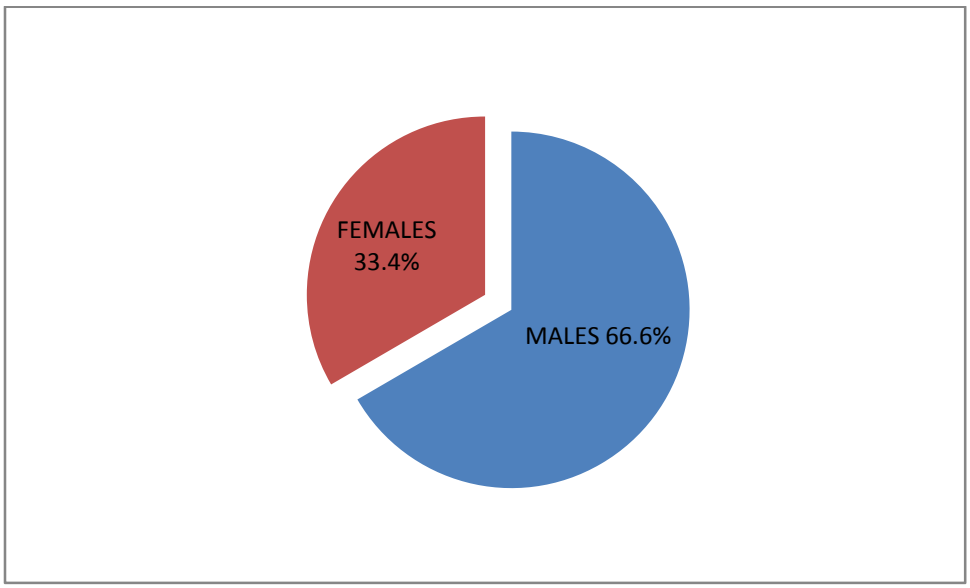
Hypersplenism was diagnosed in 13 cases.

The mean age for hypersplenism was 40.6 years with a male to female ratio of 1.6:1

In almost all patients spleen was palpable (92.3%) on examination.

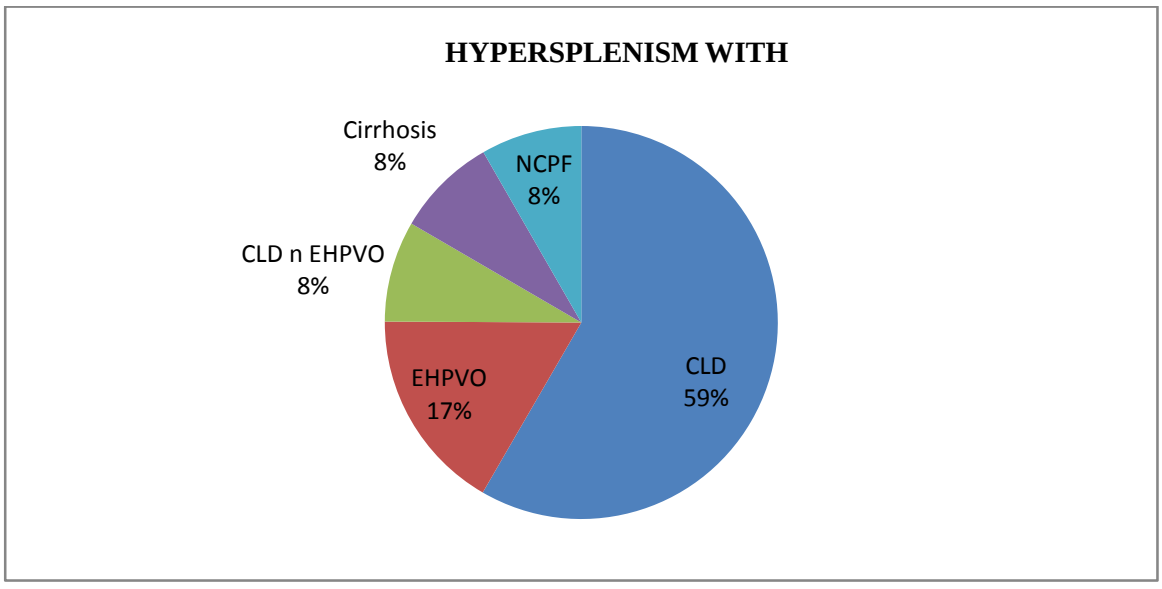
The most common peripheral smear finding of hypersplenism were MCHA (92.3%) and reticulocytosis(30.8%).

FIGURE 7.1: Sex wise distribution of hypersplenism.



Males comprised of 66.6% and females comprised of 33.4%.

FIGURE 7.2 : Pie-chart depicting the frequency of various etiological factors of hypersplenism.



CLD- chronic liver disease, EHPVO- Extra hepatic portal vein obstruction, NCPF- Non cirrhotic portal fibrosis.

CLD with portal hypertension was the most common cause(59%) followed by EHPVO, which was seen in 17% of patients. NCPF was another cause(8%) and were all female patients.

CONNECTION TISSUE DISEASE

SLE was diagnosed in 3 cases of pancytopenia out of which 2 were female and 1 was a male patient.

ACUTE LEUKEMIA

Acute myeloid leukemia comprised of 3 cases out of which 2 were female and 1 male, while Acute lymphoblastic leukemia comprised of 2 cases, 1 male and 1 female.

DENGUE

4 cases of dengue was diagnosed out of which 2 were male and 2 female. All of them presented with some form of bleeding manifestation.

MALARIA

Malaria was diagnosed in 4 cases of patients in our study, 3 males and 1 female. All of the patients was diagnosed to have plasmodium vivax malaria.

VIRAL INDUCED PANCYTOPENIA

2 cases was diagnosed as viral induced pancytopenia, 1 male and 1 female.

DISSEMINATED TB

1 male patient had disseminated TB.

HIV

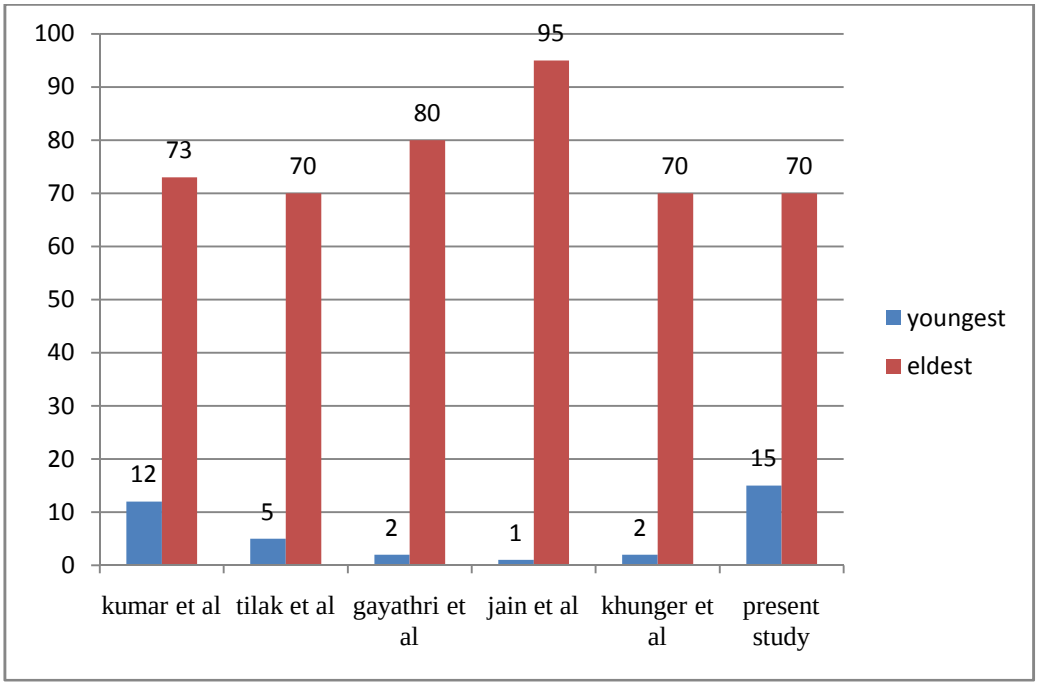
1 male patients was diagnosed to have HIV.

DISCUSSION

Pancytopenia is not an uncommon hematological problem that we face in our daily practise. It is not a disease per se but rather a triad of findings that consists of anaemia, leucopenia and thrombocytopenia. Peripheral pancytopenia can be caused by a wide variety of conditions that primarily or secondarily affect the bone marrow. The incidence and prevalence of these various etiologies depend on a number of factors like the geographic location, population groups, nutritional status, exposure to drugs etc.

In our study, 100 patients were studied and evaluated for various etiologies and their clinical presentation. The age group varied from 15-70 years, with a mean age of 40 years.

Figure 8.1: Comparison in age group with other studies and present study.



Males were found to have a slight preponderance in the incidence of pancytopenia in our study with a male to female ratio of 1.3:1 which is comparable to other studies described below.

Figure 8.1: Comparison of male to female ratio with other studies.

STUDY AUTHOR	MALE:FEMALE RATIO
Savage PG et al[54]	1.3:1
Kumar et al[11]	2.1:1
Gayathri et al[55]	1.2:1
Khunger et al[15]	1.2:1
Kodke et al	1.3:1
Present study	1.3:1

In our study, the most common etiology was megaloblastic anaemia (37%) followed by aplastic anaemia(24%), hypersplenism(12%) and myelodysplastic syndrome(6%).

A comparison of studies between southern, northern, western and eastern India on the four most common etiology of pancytopenia is described below.

TABLE 8.2: Comparison of studies in dIfferent region of India on most common etiology.

Author	Region	Year	1st Common	2nd Common	3rd Common	4th Common
Dubey et al [60] (n=248)	Central India, MP	2015	Megaloblastic anaemia(41.4%)	Aplastic anaemia(22.9)	Hypersplenism (12.9%)	AML (2.4%)
Vaddatti Tejeswini et al [65] (n=75)	South India, AP	2015	Megaloblastic anaemia (68%)	Aplastic anaemia (13.3%)	Leukemia & MDS (both 5.34%)	ITP (4%)
Neha Sharma et al [56] (n=100)	Jammu & kashmir	2017	Megaloblastic anaemia (60%)	Aplastic anaemia (16%)	ALL (11%)	AML(4%)
Dasgupta et al [66] (n=70)	East India, WB	2018	Aplastic anaemia (33.4%)	Megaloblastic anaemia (20.9%)	Kala azar (13.7%)	TB (4.8%)
Patel et al [67] (n=50)	West India, Gujarat	2017	Megaloblastic anaemia (58%)	Aplastic anaemia (12%)	Hypersplenism (8%)	Leukemia (6%)
Current study (n=100)	South India, TN	2018	Megaloblastic anaemia (37%)	Aplastic anaemia (24%)	Hypersplenism (13%)	MDS (6%)

ALL- acute lymphoblastic leukemia, AML- acute myeloid leukemia, AP-andhra Pradesh,MDS- myelodysplastic syndrome, MP-madhya Pradesh, TB-tuberculosis, WB- west Bengal.

The most common symptom at presentation in our study was easy fatigueability (91%) followed by anorexia(60%), Fever(57%) and bleeding manifestation (37%). Similar results were observed in studies described below.

TABLE 8.3: Comparison of studies on most common symptoms at presentation.

Study	Easy fatigue %	Dypnea %	Fever %	Bleed %
Pereira & Dias et al [61] (n=80)	37.5	30	35	15
Reddy GP et al [63] (n=42)	26.2	59.5	45.2	7.1
Gayathri et al [55] (n=104)	100	43.2	38.4	3.84
Majed momin et al [62] (n=150)	54	24.6	68.6	8
Hema goyal et al [59] (n=140)	90		61.4	40
Current study (n=100)	91	52	57	35

On physical examination, the most common finding was palor which was found in 97% of patients as opposed to other studies by Gayathri et al [55], Pereira & Dias et al[61], Majed momin et al [62] where palor was present in 100% of patients. In our study three of the them were diagnosed to have dengue had their haemoglobin was in the range of 11-12g/dl. The second most common finding was splenomegaly(27%), hepatomegaly(15%) and icterus(11%) which was comparable to other studies conducted by Gayathri et al [55], Pereira & Dias et al[61], Majed momin et al [62] and Bhaskar B. Thakkar et al[64].

TABLE 8.4: Comparison of studies on most common physical finding.

Study	Palor %	Icterus %	Splenomegaly %	Hepatomegaly %	Lymphadenopathy %
Gayathri et al [55] (n=104)	100	3.82	35.5	26.9	0.98
Bhaskar B. Thakkar et al[64] (n=100)	100	11	23	17	3
Pereira & Dias et al [61] (n=80)	100	6.2	32.5	20	7.5
Majed momin et al [62] (n=150)	100	10.6	36.6	10.6	4.6
Current study	97	11	27	15	3

Megaloblastic anaemia was found to be the most common etiology of pancytopenia in our study (37%) which was comparable to other studies in different regions of India by Dubey et al [60], Vaddatti Tejeswini et al [65], Neha Sharma et al [56], Patel et al [67], Gayathri et al [55], Bhaskar B. Thakkar et al[64], Pereira & Dias et al [61] and Majed momin et al [62]. However Studies by Dasgupta et al [66] conducted in kolkata, Santra G et al[70] and international agranulocytosis & aplastic anaemia study group in Israel & Europe[71] found aplastic anemia to be the most common etiology.

Among the megaloblastic anaemia, the male to female ratio was 1.3:1 and 29.7% were found to consume vegetarian diet which may be responsible

for the deficient state. Among the male cases of megaloblastic anaemia, 42% were either alcoholic or smoker or both.

Almost all patients of megaloblastic anemia presented with easy fatigueability (100%), fever was the next common presenting complaint (48.6%) and 13.5% of these patients had some bleeding manifestation which was comparable to other studies by Hema goyal et al [59, Neha Sharma et al [56], Patel et al [67], Gayathri et al [55], Bhaskar B. Thakkar et al[64].

In the peripheral smear study, 76% of the patients showed macrocytosis with MCV>100, hypersegmented neutrophils was found in 90% and 74% of patients had LDH of >500 comparable to other studies by Para R et al [57], Eivazi-ziaei J et al [58], Tilak et al[3] , Khunger et al[15] and Ishtiaq et al[68].

Most of the megaloblastic anemia in our study had Vitamin B12 deficiency alone (59.4%), 18.9% had folate deficiency alone and 16.2% had both vitamin B12 and Folate deficiency. Similar results were shown in the study done by Aziz et al[69].

Bone marrow study was deferred in most of the cases of megaloblastic anemia since most of the cases were diagnosed on history, examination, peripheral smear and vitamin B12 and folate analysis. Bone marrow study may show typical megaloblasts with sieved chromatin and asynchronic nuclear cytoplasmic ratio.

In almost all age group in our study, megaloblastic anemia was found to be the major cause of of pancytopenia and were found to have some deficient

state. This reflects on the nutritional status as an important cause of pancytopenia in our society.

Aplastic anaemia was found to be the 2nd most common cause of pancytopenia in our study and comprised of 24% of cases with a male to female ratio of 1.1:1. Some other studies conducted in India by Dasgupta et al [66] and Santra G et al[70] and international agranulocytosis & aplastic anaemia study group in Israel & Europe[71] found aplastic anaemia to be the most common etiology of pancytopenia.

The incidence was higher in the age group >50 years(45.8%) and <20 years(20.8%) and reflects on the bimodal age distribution of aplastic anemia[27], although it can be found in all age groups. Most of them presented with easy fatigueability(87.5%), bleeding manifestation(58.3%) and fever(54.1%).

A 15 year old female had microcephaly, bifid thumbs, short stature and cafe-au-lait spots with bone marrow study showing hypoplasia. She was subsequently diagnosed as Fanoni anaemia.

A 21 year old male presented with fever, shortness of breath, cough, redness of right eye and increased pigmentation of palms and soles for 2 weeks. On further history, he admits that he was abused with glue sniffing(dendrite) for 8 years and stagbond(toluene) for 1 month. On evaluation he was found to have low vitamin B12 and low cortisol with bone marrow study showing hypocellularity and atypical blastoid cells. He was then diagnosed as Toulene

induced hypoplasia and megaloblastic anaemia as the cause of pancytopenia. Thus such addiction histories are important to ask when the diagnosis is in doubt.

Hypersplenism was the 3rd most common etiology in our study(13%) with a mean age of 40.6 years and male to female ratio of 1.6:1. Most of them had chronic liver disease(CLD) with portal hypertension(61%). Two cases were found to be HCV positive and 1 case HBV positive as the cause for CLD while the rest were ethanol related CLD. Extrahepatic portal vein obstruction (EHPVO) was found in 17% as the cause of hypersplenism. Two female cases had non cirrhotic portal fibrosis(NCPF) and both of them has massive splenomegaly.

This findings in contrast to earlier studies done by Hamid GAet al[72] and Kale Pet al [73] where they found hypersplenism as the most common cause for pancytopenia. Since those studies were done more than a decade ago, the better diagnosis and treatment of Malaria and Kala azar might have lead to the decreased incidence of these diseases in our study.

The incidence of myelodysplastic syndrome is 6% in our study . Most of the patients are above 50 years . Hyposegmented neutrophils were seen in the peripheral smear of two patients with MDS. Diagnosis was confirmed by bone marrow study showing hypercellularity with abnormal cells. In these patients malignancy, monoclonal gammopathies were ruled out by appropriate

investigations. Serum folate and vit B12 levels were normal in all the patients with MDS in our study.

Three patients were diagnosed to have SLE out of which one was a male patient. He presented with musculoskeletal and mucocutaneous features with malar rash, joint pain, oral ulcer and alopecia. He was subsequently found to have Lupus Nephritis of Grade 5. Thus haematological abnormality such as pancytopenia in male SLE should be evaluated further for renal involvement. Both the female cases in our study did not have renal involvement.

Acute leukemia was diagnosed in 5 cases in our study. 3 patients had AML and 2 case ALL. This in contrast to other studies done in western country and Europe where acute leukemia as the most common etiology of pancytopenia-Weinzieri EP et al[74], Imbert et al[76].

Tropical infections such as dengue(4%) and malaria(4%) were also diagnosed in our study. All the cases of malaria were positive for vivax malariae. A study conducted in Pakistan by Tareem SM et al[75] found malaria as the most common etiology of pancytopenia. Thus these infections should also be kept in mind while dealing with pancytopenia cases especially in endemic areas.

Immunocompromised states such as with HIV infection were found in 2 cases. One patient had disseminated TB with bone marrow involvement. He eventually succumbed to sepsis and expired. This explains the seriousness of pancytopenia in such patients.

CONCLUSION

- In India, megaloblastic anaemia was found to be the most common etiology for pancytopenia according to several studies done in different parts of the country.
- Similarly in our study, megaloblastic anaemia was found to be the most common cause for pancytopenia.
- Most of them had either Vitamin B12 or Folate deficiency or both, thus reflecting the poor nutritional status of a developing country as India. This issue needs to be addressed so that the incidence of pancytopenia and thus its complications can be prevented with simple measures like dietary advice and timely supplementation. Also in our study, males tends to be affected more than females which could be due to the reason that most of them had ethanol abuse and its related CLD which may contribute to the deficient state.
- The diagnosis and high index of suspicion of these cases can be made when a patient presents with easy fatigueability, fever or bleeding manifestation with hepatomegaly or splenomegaly or both and peripheral smear study showing macrocytosis and hypersegmented neutrophils with decreased serum Vitamin B12 and folate assays. In such cases bone marrow studies can be deferred and can be treated with hematinics(Vitamin B12/Folate) with close haematological follow up.
- Aplastic anaemia was the 2nd most common etiology in our study with slight male preponderance. The disease was found to be bimodal in

distribution. Blood counts were very low in such cases and all had hypoplastic marrow. Secondary cause of aplasia such as exposure to drugs and chemicals like toluene should be always sought for before labelling as primary disease.

- Hypersplenism is another important cause in our study. Chronic liver disease with portal hypertension was the major contributing factor.
- Myelodysplastic syndrome should be suspected in elderly population with unexplained anaemia with pancytopenia. Bone marrow should be done to rule out malignancy.
- Tropical infections such as dengue and malaria should always be ruled out especially in endemic areas.
- Additional tests such as ANA, viral studies etc. should be considered when diagnosis is in doubt after ruling out the most common causes.
- As our study also found megaloblastic anaemia as the most common cause comparable to other studies in different parts of our country, we may conclude that a major cause of pancytopenia in our country can be prevented and treated.

LIMITATION OF STUDY

- The study group was small and was done in patients admitted to tertiary care hospital and thus the exact number and etiology in the general population cannot be assessed.
- Some investigations such as intrinsic factor and some viral studies were not done to search for the cause of pancytopenia.
- Trephine biopsy evaluation was not done in all patients. Therefore more definitive evaluation of cellularity and exclusion of focal lesions could not be done.
- Follow up of patients was not done and so response to therapy could not be assessed.

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ANNEXURES

ETHICS COMMITTEE APPROVAL

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To

Dr.Nokchur Imchen - [illegible]
I Year PG in MD General Medicine
Institute of Internal Medicine
Madras Medical College
Chennai 600 003

Dear Dr.Nokchur Imchen,

The Institutional Ethics Committee has considered your request and approved your study titled **"CLINICAL AND ETIOLOGICAL PROFILE OF PANCYTOPENIA IN TERTIARY CARE HOSPITAL "** - **NO.13062017(A)**

The following members of Ethics Committee were present in the meeting hold on 20.06.2017 conducted at Madras Medical College, Chennai 3

1. Prof.Dr.C.Rajendran, MD.,	:Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., MMC,Ch-3	: Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	:Member Secretary
4. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3	: Member
5. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC	: Member
6. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai	: Member
7. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3	: Member
8.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
9.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist
10.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

13/12/17

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE

PLAGIARISM

URKUND

Urkund Analysis Result

Analysed Document:	PANCYTOPENIA. CLINICAL AND ETIOLOGICAL PROFILE IN TERTIARY HEALTH CARE.docx (D42538951)
Submitted:	10/14/2018 8:59:00 PM
Submitted By:	anokmjn@gmail.com
Significance:	6 %

Sources included in the report:

new word rol.docx (D31652735)
from introduction to conclusion 98 pages.docx (D42039687)
Aviral Chandra Thesis A clinicohematological study of pancytopenia.docx (D30728504)
CHILDREN WITH BICYTOPENIA AND PANCYTOPENIA -.doc (D31621286)
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Children with bicytopenia and pancytopenia clinical etiological spectrum.docx (D31230035)
thesis full.pdf (D41796582)
plagiarism check.docx (D30718446)

Instances where selected sources appear:

30

PROFORMA

1. Name:
2. Age:
3. Sex:
4. Ip No:
5. Symptoms
    a. Easy Fatigueability
    b. Fever
    c. Bleeding Manifestation
    d. Bone Pain
    e. Night Sweats
    f. Weight Loss
    g. Pruritus
    h. Others
6. Dietary Habits:
7. Smoking Status:
8. Alcohol Consumption:
9. Treatment History:
10. Intake Or Exposure To Potential Toxic Chemical Agents Or Drugs
11. Radiation Exposure
12. Clinical Examination
    a. Pallor
    b. Icterus
    c. Hepatomegaly
    d. Splenomegaly
    e. Lymphadenopathy
    f. Sternal Tenderness
    g. Gum Hypertrophy
    h. Other Signs
13. Investigations
    a. CBC
        i. Hb:
        ii. TLC:
        iii. Plateletes
        iv. MCV
        v. MCH
        vi. MCHC
    b. Peripheral Blood Smear
    c. LFT
    d. LDH
    e. Ultrasound Examination
    f. Bone Marrow Examination
    g. Other Investigation

PATIENT CONSENT FORM

- Study Detail:“ PANCYTOPENIA : CLINICAL AND ETIOLOGICAL PROFILE IN TERTIARY CARE HOSPITAL”
- Study Centre: Rajiv Gandhi Government General Hospital, Chennai.
- Patient’s Name:
- Patient’s Age:
- In Patient Number:
- Patient may check (√) these boxes
- I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.❑
- I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.❑
- I understand that sponsor of the clinical study, others working on the sponsor’s behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.❑
- I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.❑
- I hereby consent to participate in this study.❑
- I hereby give permission to undergo detailed clinical examination and blood investigations as required.❑

Signature of investigator Signature/Thumb impression

Study investigator Name: Patient name and address:

ஆய்வு ஒப்புதல் படிவம்

ஆய்வு தலைப்பு :

மூன்றாவது பராமரிப்பு நிலையிலான மருத்துவமனைகளில் பேன்சைட்டோபீலியா (Pancytopenia) எனப்படும் இரத்த அணுக்கள் குறைப்பாட்டினால் ஏற்படும் நோயின் மருத்துவரீதியான மற்றும் நோய்காரணவியலின் விவரங்களை ஆராய்தல்

பெயர் :
வயது :
பால் :

தேதி :
வெளிநோயாளி எண் :
ஆராய்ச்சி சேர்க்கை எண் :

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்துகொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் மூன்றாவது பராமரிப்பு நிலையிலான மருத்துவமனைகளில் பேன்சைட்டோபீலியா (Pancytopenia) எனப்படும் இரத்த அணுக்கள் குறைப்பாட்டினால் ஏற்படும் நோயின் மருத்துவரீதியான மற்றும் நோய்காரணவியலின் விவரங்களை பற்றி ஆராயப்படுகிறது என்பதை ஆராய்ச்சியாளர் கூற அறிந்துகொண்டேன்.

மேற்கண்ட பரிசோதனையின் போது ஏற்படக்கூடிய பின்விளைவுகளையும் முழுவதும் உணர்ந்து இந்த பரிசோதனைக்கு மனமார சம்மதிக்கிறேன்.

நான் ஆராய்ச்சியாளருடன் ஒத்துழைப்பேன் என்றும், எனக்கு ஏற்படக்கூடிய ஆசாதாரண நிகழ்வுகள் பற்றியும் உடனடியாக ஆராய்ச்சியாளரிடம் தெரிவிப்பேன் என்று உறுதி கூறுகிறேன். இந்த ஆய்விலிருந்து எப்போது வேண்டுமானாலும் எக்காரணமும் கூறாமல் என்னை விடுவித்துக்கொள்ளலாம் என்பதை அறிவேன்.

என்னிடம் இருந்து பெறப்படும் தகவல்களை அரசு, வரைமுறை அதிகாரிகள் ஆகியோர்களுடன் பகிர்ந்துகொள்ள ஆராய்ச்சியாளருக்கு அனுமதி அளிக்கிறேன். என்னுடைய சிகிச்சைக்கட்டுகளை பார்வையிட உரிமை உண்டு. என்னுடைய தகவல்களின் அடையாளம் இரகசியமாக வைக்கப்படும் என்பதை அறிவேன்.

இந்த ஆராய்ச்சியில் பங்கேற்க தன்னிச்சையாக முழு மனதுடன் சம்மதிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் / ரேகை

பங்கேற்பவர் பெயர்

இடம் :

தேதி :

ஆய்வாளர் கையொப்பம்

ஆய்வாளர் பெயர்

இடம் :

தேதி :

ஆய்வு தகவல் தாள்

ஆய்வு தலைப்பு :

மூன்றாவது பராமரிப்பு நிலையிலான மருத்துவமனைகளில் பேன்சைட்டோபீலியா (Pancytopenia) எனப்படும் இரத்த அணுக்கள் குறைப்பாட்டினால் ஏற்படும் நோயின் மருத்துவரீதியான மற்றும் நோய்காரணவியலின் விவரங்களை ஆராய்தல்

ஆய்வாளர் பெயர் : மரு. நொக்சர் இம்சென்

ஆய்வு நிலையம் : பொது மருத்துவப் பிரிவு,
சென்னை மருத்துவக் கல்லூரி, சென்னை-3.

இந்த ஆய்வில் தங்களை பங்கேற்க அழைக்கிறோம். இந்த தகவல் அறிக்கையில் கூறப்பட்டிருக்கும் தகவல்கள் தாங்கள் இந்த ஆராய்ச்சியில் பங்கேற்கலாமா வேண்டாமா என்பதை முடிவு செய்ய உதவியாக இருக்கும். இந்த படிவத்தில் உள்ள தகவல்கள் பற்றி உள்ள சந்தேகங்களை நீங்கள் தயங்காமல் கேட்கலாம்.

இதில் ஆய்வின் மூலம் மூன்றாவது பராமரிப்பு நிலையிலான மருத்துவமனைகளில் பேன்சைட்டோபீலியா (Pancytopenia) எனப்படும் இரத்த அணுக்கள் குறைப்பாட்டினால் ஏற்படும் நோயின் மருத்துவரீதியான மற்றும் நோய்காரணவியலின் விவரங்களை பற்றி அறிவதற்கு தங்கள் ஒத்துழைப்புத் தேவை.

நீங்கள் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில்தான் இருக்கிறது. மேலும் நீங்கள் எந்த நேரமும் இந்த ஆராய்ச்சியில் இருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனையின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவில் தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம்

தேதி :

பங்கேற்பாளர் கையொப்பம் /
இடது கட்டைவிரல் ரேகை

தேதி :

MASTER CHART

SL. NO	AGE	SEX	EASY FATIGUEABILITY	FEVER	BLEEDING TENDENCY	BONE PAINS	NIGHT SWEATS	WEIGHT LOSS	ANOREXIA	DYSPNEA	OTHERS	DIET	SMOKING	ALCOHOL	OTHER ADDICTION
1	16	M	YES	NO	NO	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
2	24	M	YES	YES	NO	NO	NO	NO	NO	NO		MIXED	YES	YES	NO
3	55	F	NO	NO	GUMS BLEED,MALENA	NO	NO	NO	NO	NO		MIXED	NO	NO	NO
4	15	F	YES	YES	NO	NO	NO	NO	NO	NO		MIXED	NO	YES	NO
5	32	M	NO	YES	NO	NO	NO	NO	NO	NO	LOOSE STOOLS	MIXED	YES	YES	NO
6	70	M	YES	NO	HEMATEMESIS	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
7	44	M	YES	NO	NO	NO	NO	NO	NO	NO		MIXED	YES	YES	NO
8	60	M	YES	NO	GUM BLEED	NO	NO	NO	NO	NO	MYALGIA	MIXED	NO	NO	NO
9	63	M	YES	NO	NO	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
10	29	M	YES	YES	NO	NO	NO	YES	YES	YES	ORAL ULCER	MIXED	NO	YES	NO
11	42	M	YES	NO	NO	NO	NO	NO	NO	NO	JAUNDICE, VOMITING	MIXED	YES	YES	NO
12	46	M	NO	YES	NO	NO	NO	NO	NO	NO		MIXED	YES	YES	NO
13	37	M	YES	NO	NO	NO	NO	NO	NO	NO	JAUNDICE	MIXED	YES	YES	NO
14	59	F	YES	YES	NO	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
15	60	F	YES	NO	NO	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
16	50	M	NO	YES	NO	NO	NO	NO	NO	YES	B/L LEG SWELLING	VEG	YES	YES	NO
17	38	M	YES	NO	NO	NO	NO	NO	NO	YES	JAUNDICE	VEG	NO	YES	NO
18	24	M	YES	YES	NO	ARTHRALGIA	NO	YES	YES	NO	MALAR RASH, MYALGIA	MIXED	NO	NO	NO
19	33	M	YES	YES	EPISTAXIS	ARTHRALGIA	NO	NO	NO	NO	MYALGIA	MIXED	NO	NO	NO
20	44	M	YES	NO	NO	NO	NO	NO	NO	NO		VEG	YES	YES	NO
21	39	M	YES	YES	NO	NO	YES	YES	YES	NO	COUGH WITH EXP.	MIXED	YES	NO	NO
22	63	F	YES	NO	NO	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
23	26	F	YES	YES	NO	NO	NO	NO	NO	NO	MYALGIA	MIXED	NO	NO	NO
24	45	M	YES	NO	HEMATEMESIS, MALENA	NO	NO	YES	YES	YES		MIXED	YES	YES	NO
25	50	M	YES	YES	NO	NO	NO	NO	NO	NO	JAUNDICE	VEG	NO	NO	NO
26	60	M	YES	NO	NO	NO	NO	YES	YES	NO		MIXED	NO	NO	NO
27	40	F	YES	NO	NO	NO	NO	YES	YES	NO		VEG	NO	NO	NO
28	52	F	YES	NO	NO	NO	NO	NO	NO	NO		VEG	NO	NO	NO
29	52	M	YES	NO	NO	NO	NO	NO	YES	NO		MIXED	YES	YES	NO
30	50	F	YES	YES	NO	NO	YES	NO	NO	NO		MIXED	NO	NO	NO
31	44	F	YES	YES	NO	NO	NO	NO	NO	NO		VEG	NO	NO	NO
32	53	M	YES	YES	MALENA	NO	NO	NO	YES	YES		MIXED	NO	YES	NO
33	19	M	YES	NO	MALENA	NO	NO	YES	NO	YES		MIXED	NO	NO	NO
34	38	F	YES	YES	HEMATEMESIS, MALENA	NO	NO	NO	YES	NO	JAUNDICE	MIXED	NO	NO	NO
35	22	F	NO	NO	PETECHIAE	ARTHRALGIA	NO	NO	YES	NO		MIXED	NO	NO	NO
36	40	F	YES	NO	HEMATEMESIS, MALENA	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
37	45	F	YES	NO	NO	NO	NO	NO	YES	NO	ANGULAR STOMATITIS	VEG	NO	NO	NO
38	38	M	YES	NO	NO	NO	NO	YES	YES	YES		MIXED	YES	YES	NO
39	48	M	YES	YES	NO	NO	NO	NO	YES	YES		MIXED	NO	YES	NO
40	21	F	YES	YES	HEAVY MENS	NO	NO	YES	YES	YES		VEG	NO	NO	NO
41	19	M	YES	YES	GUM BLEED	NO	NO	YES	YES	YES		MIXED	NO	NO	NO
42	40	F	YES	YES	EASY BRUISABILITY	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
43	36	M	YES	NO	MALENA	NO	NO	YES	YES	NO		MIXED	YES	YES	NO
44	52	F	YES	NO	NO	NO	NO	NO	NO	NO		MIXED	NO	NO	NO
45	30	M	YES	YES	NO	NO	NO	NO	NO	NO		MIXED	NO	NO	NO
46	46	F	YES	YES	NO	NO	NO	YES	YES	NO	JAUNDICE	MIXED	NO	NO	NO
47	42	M	YES	NO	HEMATEMESIS, MALENA	NO	NO	YES	YES	YES	JAUNDICE	MIXED	YES	YES	NO
48	58	M	YES	YES	NO	NO	NO	NO	YES	YES		MIXED	YES	YES	NO
49	60	F	YES	NO	NO	NO	NO	YES	YES	NO		MIXED	NO	NO	NO
50	56	M	YES	YES	NO	NO	YES	YES	YES	YES		MIXED	YES	YES	NO
51	45	F	YES	YES	GUM BLEED, EPISTAXIS	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
52	25	M	YES	NO	MALENA	NO	NO	NO	YES	NO		MIXED	NO	NO	NO
53	38	F	YES	YES	NO	ARTHRALGIA	YES	NO	YES	YES	ALOPECIA	MIXED	NO	NO	NO
54	63	F	YES	NO	NO	NO	NO	NO	YES	YES		MIXED	NO	NO	NO
55	35	M	YES	YES	NO	NO	NO	NO	YES	NO	JAUNDICE	VEG	NO	NO	NO
56	16	M	YES	YES	GUM BLEED	NO	NO	NO	YES	NO		MIXED	NO	NO	NO
57	37	F	YES	NO	NO	NO	NO	NO	YES	YES		MIXED	NO	NO	NO
58	38	M	YES	YES	EASY BRUISE	NO	NO	NO	YES	YES		MIXED	YES	YES	NO
59	28	M	YES	NO	NO	NO	NO	YES	YES	NO		MIXED	NO	NO	NO
60	36	F	YES	YES	NO	NO	NO	YES	YES	YES	MYALGIA	VEG	NO	NO	NO
61	28	M	YES	YES	EPISTAXIS	ARTHRALGIA	NO	NO	YES	NO	MYALGIA	MIXED	YES	NO	NO
62	18	F	YES	YES	NO	NO	NO	NO	YES	NO		MIXED	NO	NO	NO
63	65	F	YES	NO	NO	NO	NO	YES	YES	YES		MIXED	NO	NO	NO
64	17	F	YES	YES	NO	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
65	34	M	YES	NO	MALENA	NO	NO	YES	YES	NO		MIXED	NO	NO	NO
66	55	F	YES	YES	NO	NO	NO	NO	YES	YES	HYPERPIGMENTED KNUCKLES	MIXED	NO	NO	NO
67	68	M	YES	YES	EPISTAXIS	NO	NO	NO	YES	YES		MIXED	YES	YES	NO
68	17	M	YES	YES	NO	NO	YES	YES	YES	YES		MIXED	NO	NO	NO
69	28	M	YES	NO	NO	NO	NO	NO	YES	NO	JAUNDICE	MIXED	YES	NO	NO
70	43	M	YES	YES	NO	NO	NO	NO	NO	YES		MIXED	NO	NO	NO
71	58	F	YES	NO	NO	NO	NO	NO	NO	NO		MIXED	NO	NO	NO
72	25	F	YES	YES	HEAVY MENS	NO	NO	YES	YES	NO	GLOSSITIS, HYPERPIGMENTED KNUCKLES	VEG	NO	NO	NO
73	40	M	YES	YES	HEMATEMESIS, MALENA	NO	NO	YES	YES	YES	JAUNDICE	MIXED	YES	YES	NO
74	50	F	YES	YES	NO	NO	NO	YES	YES	YES		MIXED	NO	NO	NO
75	48	M	YES	NO	MALENA	NO	NO	YES	YES	YES	JAUNDICE	MIXED	YES	YES	NO
76	15	M	YES	YES	NO	NO	YES	NO	YES	YES		MIXED	NO	NO	NO
77	21	M	YES	YES	NO	NO	NO	NO	NO	NO		MIXED	NO	NO	NO
78	39	M	YES	NO	MALENA	NO	NO	YES	YES	YES	JAUNDICE	MIXED	YES	YES	NO
79	58	M	YES	YES	NO	NO	NO	NO	YES	YES		MIXED	NO	NO	NO
80	35	M	YES	YES	MALENA	NO	NO	NO	YES	YES		MIXED	YES	YES	NO
81	37	M	YES	NO	NO	NO	NO	NO	YES	NO		MIXED	NO	NO	NO
82	58	M	YES	NO	EASY BRUISABILITY	NO	NO	YES	YES	YES		MIXED	NO	YES	NO
83	28	F	YES	YES	NO	NO	NO	YES	YES	YES		MIXED	NO	NO	NO
84	20	M	YES	YES	EPISTAXIS	NO	NO	NO	NO	YES		VEG	NO	NO	NO
85	52	F	YES	NO	NO	NO	NO	YES	YES	YES		MIXED	NO	NO	NO
86	39	F	YES	YES	NO	NO	NO	YES	YES	NO	GLOSSITIC	MIXED	NO	NO	NO
87	31	M	YES	NO	NO	NO	NO	NO	NO	NO	ANGULAR STOMATITIS	MIXED	YES	YES	NO
88	26	F	YES	YES	EASY BRUISE, HEAVY MENS	NO	NO	NO	YES	YES		MIXED	NO	NO	NO
89	33	F	NO	YES	PETECHIAE	NO	NO	NO	NO	NO		MIXED	NO	NO	NO
90	20	M	NO	YES	NO	NO	NO	NO	YES	NO		MIXED	NO	NO	NO
91	60	F	NO	NO	NO	NO	NO	NO	YES	YES	ABDOMINAL DISTENSION	MIXED	NO	NO	NO
92	30	F	YES	NO	EPIXTAXIS	NO	NO	NO	YES	NO		MIXED	NO	NO	NO
93	40	F	YES	YES	NO	NO	NO	NO	NO	NO		MIXED	NO	NO	NO
94	48	F	YES	YES	EASY BRUISABILITY	ARTHRALGIA	YES	YES	YES	YES		MIXED	NO	NO	NO
95	21	M	NO	YES	NO	NO	NO	NO	NO	YES	REDNESS OF EYES, HYPERPIGMENTATION OF PALMS	MIXED	NO	NO	GLUE SNIFFER,STAFBOND
96	50	M	YES	YES	NO	NO	NO	NO	YES	YES		VEG	YES	YES	NO
97	60	F	YES	YES	EASY BRUISABILITY	NO	NO	YES	YES	YES		MIXED	NO	NO	NO
98	42	M	YES	NO	MALENA	NO	NO	YES	YES	YES		MIXED	YES	YES	NO
99	26	F	YES	YES	NO	NO	NO	NO	NO	NO		MIXED	NO	NO	NO
100	45	F	YES	YES	NO	NO	NO	NO	YES	YES	HYPERPIGMENTED KNUCKLES	MIXED	NO	NO	NO

SL. NO	HB (g/dl)	PCV	TLC	PLAT	MCV (fl)	MCH (pg)	MCHC (g/dl	TB	OT	PT	ALP	TP	RC	LDH	USG	VIT B12	FOLATE
1	3.4	10	2000	13000	102.9	33.3	32.4	0.8	21	23	45	6.2	<0.5 %		NORMAL		
2	7.3	21	2700	79000	101.9	34.9	34.3	0.7	22	23	40	5.6	2%		NORMAL	154 (DECREASED)	>24 (NORMAL)
3	8.1	25	3700	21000	100	32.5	31.2	0.8	30	23	45	5.4	0.10%		NORMAL		
4	4	11	2500	21000	99	35	36	0.7	40	45	56	5.7	<0.5%		NORMAL		
5	11	30	2600	52000	85.2	30.7	36	0.5	21	23	30	5.4	1.90%		NORMAL		
6	5.4	15	1500	7000	96.7	34.4	35.5	0.7	30	32	38	6.2	0.20%		NORMAL		
7	3.3	11	2300	90000	109.1	22.9	29.3	0.7	25	26	40	5.5	1.80%		NORMAL	500 (NORMAL)	3 (DECREASED)
8	7.4	20	1900	10000	81.6	30.3	37.2	0.6	12	21	23	5.4	0.30%	6976	NORMAL		
9	4.6	12	3600	6000	93	24	37	0.9	23	30	33	5.9	0.20%		NORMAL		
10	6.8	19	1200	23000	76.7	27.3	35.6	0.8	33	35	45	5	0.60%		SPLENOMEGALY		
11	3.5	9	2700	40000	128	33	36.5	1.1	55	45	60	4.5	1.80%	1326	GR-1 FATTY LIVER	125 (DECREASED)	<0.4 (DECREASED)
12	12	35	3100	57000	97.6	32	33.9	0.8	25	45	56	5.8	2%		NORMAL		
13	3.9	12	2700	27000	100.7	31.1	30.9	1.3	66	64	110	5.3	1.90%	4466	HSM	115(DECREASED)	3.9(DECREASED)
14	7.8	23	3400	28000	88.7	29.4	33.2	0.8	42	43	45	5.5	0.80%		NORMAL	569(NORMAL)	>24(NORMAL)
15	7.7	23	1900	24000	81.2	26.8	33	0.7	23	24	30	5.1	0.20%	203	NORMAL	425(NORMAL)	
16	3.2	9	1500	7000	100	32.7	33	1.5	56	45	66	4.2	1.80%	1073	GR-1 FATTY LIVER	112(DECREASED)	2.5(DECREASED)
17	4.9	13	1800	47000	115.7	31.3	36.6	1.6	93	80	112	4.8	2%	1279	SPLENOMEGALY	133(DECREASED)	3.4(DECREASED)
18	10.9	30	1500	51000	96	30	36	1.5	66	60	123	4.8	1%		NORMAL		
19	11	30	3500	80000	90.6	30.5	35.5	0.7	25	26	54	6.1	1.90%		GB WALL EDEMA		
20	8.5	23	3800	90000	101	29	36.9	1.4	56	58	120	5.8	1.90%	754	GR-1 FATTY LIVER	358(NORMAL)	1.2(DECREASED)
21	7.6	24	2500	65000	80.5	25	31.6	1.1	46	45	84	5.4	0.40%		HSM		
22	6.2	25	2000	12000	85.3	25.6	24.8	0.8	24	22	56	5.2	0.20%		NORMAL	256(NORMAL)	NORMAL
23	10	30	3500	60000	86.8	31.5	33.3	1.2	43	41	54	5.6	1.50%		HEPATOMEGALY		
24	4.5	18	2200	39000	100	29.5	25	0.9	40	44	56	5.4	2.10%	690	SPLENOMEGALY	310(NORMAL)	4.8(DECREASED)
25	4.1	16	3300	28000	120	30.3	25.6	3	60	35	55	5.8	0.90%	2618	NORMAL	130 (DECREASED)	>24(NORMAL)
26	6.2	19	2400	40000	91	28.3	32.6	1.8	45	45	54	5.6	0.70%	567	NORMAL		
27	1.6	5	2200	4000	82.8	26	32	0.7	33	22	40	6.1	0.20%	134	MILD HEPATOMEGALY		
28	7.2	21	3000	94000	110.2	33	34.5	0.6	31	26	43	5.1	0.90%	678	NORMAL	131(DECREASED)	11.3(NORMAL)
29	3.5	12	3100	79000	108.3	31.1	29.1	0.8	105	163	171	5.6	1.20%	1034	NORMAL	391(NORMAL)	3.9(DECREASED)
30	9.2	33	3200	120000	91.5	26.9	27.8	0.9	44	34	35	5.2	0.80%	778	NORMAL	245(NORMAL)	9.9(NORMAL)
31	5	21	2900	111000	114.2	31.2	23.8	0.6	44	53	34	5.4	0.90%	665	NORMAL	156(DECREASED)	6.1(NORMAL)
32	6.1	19	3600	40000	83.2	26.3	32.1	0.8	60	32	43	5.2	0.30%	135	NORMAL		
33	5.1	16	2500	12000	88.6	29	31.8	0.6	22	25	35	6.1	0.10%	117	NORMAL	196(DECREASED)	23(NORMAL)
34	5.6	19	2600	86000	74.2	20.2	29.4	2	160	186	155	6.9	2.80%	209	CLD,SPLENOMEGALY		
35	11	35	3400	20000	88.1	30.5	31.4	0.8	42	40	53	6	0.80%	156	NORMAL		
36	4.1	18	2000	60000	87.5	22.6	22.7	1.1	43	39	69	5.9	0.20%	93	SPLENOMEGALY		
37	7.1	21	3500	85000	112.2	32.4	33.8	0.5	15	35	45	5.5	0.60%	756	NORMAL	180(DECREASED)	10.2(NORMAL)
38	4.1	13	2000	95000	118.5	30.5	31.5	2.9	96	55	122	5.2	1.20%	927	HSM	181(DECREASED)	12.2(NORMAL)
39	4.8	14	2500	44000	93.8	30.6	34.2	0.8	32	44	51	6.2	0.90%	556	NORMAL	185(DECREASED)	7.2(NORMAL)
40	3.4	11	3400	6000	98.3	30.5	30.9	0.7	22	35	50	6.2	0.50%	125	NORMAL		
41	3.9	12	1900	3000	91.5	28.4	32.5	0.9	35	29	49	5.4	0.60%	78	NORMAL		
42	2.1	6	2700	3000	87.3	29.5	35	1.4	68	70	103	5.4	1.50%	156	HSM		
43	9.7	32	3100	50000	105.1	28.2	30.3	1.1	85	70	114	6.1	1.20%	451	NORMAL	180(DECREASED)	8.1(NORMAL)
44	6.9	22	3100	69000	104.1	31.3	31.3	0.8	46	32	60	6	0.70%	661	NORMAL	220(NORMAL)	3.1(DECREASED)
45	11.4	34	3200	56000	87.5	25.9	33.5	0.6	15	23	34	6.4	2.10%	231	MILD HEPATOMEGALY		
46	5.4	20	2200	76000	102.5	27.5	27	4.5	256	280	318	5.8	1.70%	184	HSM		
47	7	25	2300	79000	74.5	20.5	28	5.2	167	90	280	4.8	1.90%	330	LENOMEGALY,CIRRHOSIS		
48	8.4	24	3600	46000	96.1	28.4	33.4	1.9	42	39	64	4.8	1.00%	887	SPLENOMEGALY	356(NORMAL)	10.8(NORMAL)
49	6.5	23	3500	38000	97.9	25.1	28.2	0.9	68	70	82	5.7	0.90%	880	MILD SPLENOMEGALY	200(DECREASED)	7.8(NORMAL)
50	2.8	9	3500	110000	80.5	24.7	31.1	1.3	56	62	78	5.6	1.40%	265	NORMAL		
51	3.8	12	2500	10000	93.1	29.9	31.6	0.7	42	31	38	5.6	0.50%	97	NORMAL		
52	11.5	32	3200	88000	95.1	25.1	35.9	1.2	120	151	142	5.3	2.60%	135	SPLENOMEGALY		
53	6	18	500	16000	87.8	26.9	33.3	2.8	130	176	155	5.4	0.70%	365	SPLENOMEGALY		
54	9.5	33	3400	26000	110.4	35	28.7	0.8	23	35	52	6.2	0.20%	96	MILD SPLENOMEGALY		
55	7.5	26	3300	130000	106.2	30.1	28.8	2.5	99	102	132	6.6	1.10%	1564	MILD SPLENOMEGALY	195(DECREASED)	10.3(NORMAL)
56	2.6	8	3300	12000	112	32.1	32.5	0.8	24	25	43	5.2	0.20%	102	NORMAL		
57	5	16	3100	95000	108.2	31.2	31.2	1.1	45	55	62	5.9	1.30%	554	MILD HSM	340(NORMAL)	4.2(DECREASED)
58	4.9	14	2300	5000	98.1	31.1	35	0.5	50	30	89	5.8	0.10%	101	NORMAL		
59	6.7	26	3300	66000	111	32.1	25.7	0.6	22	31	46	5	0.9.%	1280	NORMAL	200(DECREASED)	7.9(NORMAL)
60	6.6	21	2800	66000	113.2	32.5	31.4	1.5	45	56	52	6.3	0.8.%	1230	HSM	155(DECREASED)	3.4(DECREASED)
61	10.1	25	3400	9000	88.2	29.8	35.7	0.9	26	22	113	6.8	1.50%	211	GB EDEMA		
62	2.2	10	2000	48000	106.3	32	22	0.7	35	36	55	5.1	0.70%	864	HSM	142(DECREASED)	5.6(LOW NORMAL)
63	4.6	18	2600	128000	67.8	18	25.5	0.6	23	31	34	5.6	0.90%	890	NORMAL		
64	2.9	9	800	6000	125	33	32.2	3.9	88	85	86	6	2.50%	1720	NORMAL	140(DECREASED)	6.5(NORMAL)
65	8.8	27	3800	85000	87.5	28.1	32.5	0.9	157	159	205	5.6	2.20%	220	SPLENOMEGALY		
66	3.6	18	2900	105000	95.6	27.2	20.1	2.8	40	33	45	5.7	0.60%	670	MILD SPLENOMEGALY	191(DECREASED)	10.2(NORMAL)
67	3.3	10	1600	3000	100	32.6	33	0.8	19	22	35	6.5	0.20%	120	NORMAL		
68	7.4	23	500	18000	88.5	27.3	32.1	0.8	78	66	65	4.9	1.40%	187	HSM, LN +VE		
69	6.8	20	3000	87000	105.1	31.9	34	1.8	66	76	105	5.9	0.70%	459	MILD HEPATOMEGALY	196(DECREASED)	6.9(NORMAL)
70	5.4	19	1200	17000	96.8	31.5	28.4	1.3	44	40	58	5	0.10%	113	NORMAL		
71	6.9	21	3400	80000	101	32	32.8	1	40	38	70	5.4	1.40%	550	NORMAL	189(DECREASED)	9.3(NORMAL)
72	9.8	28	2600	8000	93.5	22.7	35	0.9	56	58	64	5.2	1.80%	173	HSM		
73	10.2	33	3400	60000	82.5	25.1	30.9	4.5	189	200	250	5	2.50%	230	SPLENOMEGALY		
74	6.7	20	2900	80000	105.1	31.2	33.5	0.8	25	32	45	5.7	1.00%	980	NORMAL	201(DECREASED)	6.2(NORMAL)
75	9.2	29	1800	26000	87.4	26.5	31.5	5.6	256	60	175	4.6	2.30%	230	LENOMEGALY,CIRRHOSIS		
76	5.1	16	4000	98000	91.1	28.9	31.5	1	35	46	50	4.9	1.50%	145	HEPATOMEGALY		
77	6.3	27	1700	51000	77.5	23.4	26.5	0.7	45	41	32	5.9	1.90%	765	NORMAL	290(NORMAL)	4.1(DECREASED)
78	3.8	15	3800	8000	81.5	27.9	25.3	6.5	235	156	285	4.8	2.50%	176	SPLENOMEGALY		
79	2.9	9	1500	10000	122.2	40.3	32.2	1.1	32	23	40	5.9	0.30%	96	NORMAL		
80	4.3	16	3400	120000	108.5	29.5	28.6	0.9	83	92	45	5.3	0.70%	354	MILD HEPATOMEGALY	184(DECREASED)	10.4(NORMAL)
81	5.7	19	2800	33000	111.8	26.8	30	0.5	44	50	45	5.6	0.80%	478	NORMAL	231(NORMAL)	9.4(NORMAL)
82	5.3	23	2500	112000	73.5	18.4	23.7	0.9	44	45	56	5.5	1.10%	378	SPLENOMEGALY		
83	10.3	30	2200	90000	88.5	28.6	34.3	0.7	35	30	44	4.9	1.20%	235	NORMAL		
84	3.6	10	2000	8000	79.5	28	34.7	0.8	88	95	105	5.3	0.40%	119	NORMAL		
85	3.3	11	2300	4000	112.3	32.1	30.8	0.9	23	24	36	5.2	0.60%	963	NORMAL	440(NORMAL)	3.4(DECREASED)
86	7.5	28	3300	76000	119.5	33.4	28.4	0.8	33	46	55	5.6	0.90%	845	NORMAL	162(DECREASED)	6.4(NORMAL)
87	3.9	13	3200	36000	127.3	33.5	30	0.6	25	35	45	4.9	1.00%	289	NORMAL	165(DECREASED)	11.11(NORMAL)
88	2.2	8	1200	10000	82.3	26.4	27.5	1.2	33	35	44	5.6	0.20%	156	NORMAL		
89	11.2	35	3900	20000	88.9	25.4	29.4	0.5	40	41	50	6.2	1.50%	112	NORMAL		
90	10.9	33	3800	98000	91.2	28.4	33	0.9	49	40	125	6.5	1.50%	124	MILD SPLENOMEGALY		
91	7.8	25.7	3600	88000	80.3	24.4	30.4	0.8	26	13	96	6	2.40%	98	CLD, GROSS ASCITES		
92	8.2	29.5	2000	35000	73.6	20.4	27.8	0.8	29	23	97	6.4	1%	86	MASSIVE SPLENOMEGALY		
93	9.7	31	3300	30000	107.5	31	31.7	1	134	155	106	5.2	0.50%	125	NORMAL		
94	3.3	11	600	1000	91.1	28.4	30	0.8	35	40	45	4.9	1.50%	201	HSM		
95	8.8	26	400	2000	92.3	30.7	33.2	1.5	77	72	62	6.5	0.90%	150	NORMAL	182(DECREASED)	>24(NORMAL)
96	4.2	15	3000	8000	105.2	25	28	1.6	130	89	150	5.3	1.00%	1156	CLD	190(DECREASED)	3.0(DECREASED)
97	7.3	22	2000	15000	93	30.2	32.3	0.5	16	19	22	6.1	0.20%	118	NORMAL		
98	3	9	1700	60000	93.5	29.1	31.3	3.8	256	345	330	4.6	1.40%	196	LENOMEGALY, CIRRHOSIS		
99	10	33	3300	60000	90.1	25.9	30.3	0.7	12	20	40	6.5	2.10%	90	NORMAL		
100	4	13	3500	120000	88.2	28.4	30.7	0.7	23	33	40	6	0.70%	789	NORMAL	200(DECREASED)	9.4(NORMAL)

SL. NO	PERIPHERAL BLOOD SMEAR	FEVER PROFILE	HIV	VIRAL MARKERS	OTHERS
1	MCHA/ MILD LEUCOPENIA/THROMBOCYTOPENIA: **PCP**	NEG	NEG	NEG	
2	MACROCYTIC ,ANISO, MACROOVALOCYTES/ LEUCO, HYPERSEGMENTED NEUTROPHILS/ ADEQUATE PLAT, CLUMP	NEG	NEG	NEG	
3	MCHA/LYMPHOCYTOSIS/ TCP: **BICYTOPENIA**	NEG	NEG	NEG	
4	SEVERE MCHA, ANISOPOIKILOCYTOSIS, PENCIL CELLS, TEAR DROP CELLS/ LEUCOPENIA/ TCP: **PCP**	NEG	NEG	NEG	
5	NCNC/NORMAL WBC/TCP 75000/ P.VIVAX TROPHOIZES +VE RING FORMS	P.VIVAX +	NEG	NEG	
6	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
7	MACROCYTIC ANEMIA ,ANISO, MACROOVALOCYTES, TEAR DROP +VE/ LEUCOPENIA/ TCP, SINGLE: **PCP**	NEG	NEG	NEG	
8	MCHA/ DECREASE, MATURE/ TCP: **PCP**	MSAT 2+	NEG	NEG	
9	MCHA,NCNC/ LYMPHOCYTOSIS/ TCP, SINGLE: **BICYTOPENIA**	NEG	NEG	NEG	
10	MICRO,MACRO,HYPO,ANISOPOIKILO,TEAR DROP, ELLIPTO,PENCIL SHAPED/ LEUCO/ TCP: **PCP**	NEG	NEG	NEG	
11	MCHA/LEUCOPENIA/PLATELETES ADEQUATE, CLUMPS: **BICYTOPENIA**	NEG	NEG	NEG	
12	NCNC/NORMAL WBC/TCP 85000/ P.VIVAX TROPHOIZES +VE RING FORMS	P.VIVAX +	NEG	NEG	
13	DIMORPHIC ANEMIA/ LEUCOPENIA, LYMPHOCYTE PREPONDERANCE/ TCP: **DIMORPHIC ANEMIA, LEUCOPENIA,T**	NEG	NEG	NEG	
14	NCNC/NORMAL WBC, LYMPHOCYTES 40%, ATYPICAL LYMP>10%/TCP: **?ITP/APLASTIC ANEMIA**	NEG	NEG	NEG	
15	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
16	MCHA, ANISOPOIKILOCYTOSIS, TEAR DROP/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
17	MCHA, ANISOPOIKILOCYTOSIS, TEAR DROP/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
18	NCNC/LEUCOPENIA/TCP: **BICYOPENIA**	MSAT 2+	NEG	NEG	ANA, dsDNA +VE
19	NCNC/NORMAL WBC/TCP: **THROMBOCYTOPENIA**	DENGUE IgM +VE	NEG	NEG	
20	MACROCYTIC/LEUCPENIA/TCP: **PCP**	NEG	NEG	NEG	
21	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	POSITIVE	NEG	
22	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
23	NCNC/NORMAL WBC/TCP 66000/ P.VIVAX TROPHOIZES +VE RING FORMS	P.VIVAX +	NEG	NEG	
24	MACROCYTIC/LEUCPENIA/TCP: **PCP**	NEG	NEG	NEG	
25	MACROCYTIC ,ANISO, MACROOVALOCYTES/ LEUCO, HYPERSEGMENTED NEUTROPHILS/ ADEQUATE PLAT, CLUMP	NEG	NEG	NEG	
26	MCHA, ANISOPOIKILOCYTOSIS/LEUCOPENIA, OCC ATYPICAL CELLS/TCP, GIANT PLAT: **PCP**	NEG	NEG	NEG	
27	SEVERE MCHA, ANISOPOIKILOCYTOSIS/ LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
28	NCNC, MACROCYTIC, ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS	NEG	NEG	NEG	
29	MACROCYTES, HYPERSEGMENTED NEUTROPHILS	NEG	NEG	NEG	
30	NCNC,MACROCYTIC, ANISOPOIKILOCYTOSIS, ERYTHROBLAST/ HYPERSEGMENTED NEUTROPHILS/TCP,	NEG	NEG	NEG	
31	MACROCYTES,ERYTHROBLAST, ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP,CLUMPS: **PCP**	NEG	NEG	NEG	
32	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
33	NCHC/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
34	MCHA	NEG	NEG	NEG	
35	NCNC/LEUCOPENIA, LYMPHOPENIA/TCP: **BICYTOPENIA**	DENGUE IgM +VE	NEG	NEG	
36	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	PORTAL DOPPLER PHT
37	MACROCYTES,ERYTHROBLAST, ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP,CLUMPS: **PCP**	NEG	NEG	NEG	
38	MACROCYTES,ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP: **BICYTOPENIA**	NEG	NEG	NEG	
39	MACROCYTIC, ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP: **PCP**	NEG	NEG	NEG	
40	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
41	MCHA/LEUCOPENIA/TCP: **SEVERE PANCYTOPENIA**	NEG	NEG	NEG	
42	MYELOBLAST +VE	NEG	NEG	NEG	
43	NCNC, MACROCYTIC, ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/ TCP, CLUMPS +VE: **PCP**	NEG	NEG	NEG	
44	MACROCYTES, ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP: **PCP**	NEG	NEG	NEG	
45	NCNC/MILD LYMPHOCYTOSIS	NEG	NEG	NEG	
46	MCHA/LEUCOPENIA/CLUMPS	NEG	NEG	ANTI HCV +VE	
47	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
48	MCHA, TARGET CELLS	NEG	NEG	NEG	
49	MACROCYTIC, ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP: **PCP**	NEG	NEG	NEG	
50	MCHA	NEG	POSITIVE	NEG	
51	MICRO/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
52	MCHA, NORMO RBC, RETICULOCYTOSIS	NEG	NEG	NEG	PORTAL DOPPLER EHPVO
53	MCHA	NEG	NEG	NEG	ANA, dsDNA +VE
54	NCNC, MILD ANISOPOIKILOCYTOSIS, TEAR DROP CELLS/ LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
55	NORMO, MACROCYTIC,ANISOPOIKILOCYTOSIS, ERYTHROBLAST/HYPERSEGMENTED NEUTROPHILS/TCP: **BICYTOPE**	NEG	NEG	NEG	
56	MICRO,MACRO,HYPO,ANISOPOIKILOCYTOSIS/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
57	MACROCYTIC, ERYTHROBLAST/HYPERSEGMENTED NEUTROPHILS/TCP: **BICYTOPENIA**	NEG	NEG	NEG	
58	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
59	MACROCYTIC, ANISOPOIKILOCYTIC/LEUCOPENIA:	NEG	NEG	NEG	
60	ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP: **PCP**	NEG	NEG	NEG	
61	NCNC/RELATIVE LYMPHOCYTOSIS/TCP	DENGUE IgM +VE	NEG	NEG	
62	ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP: **PCP**	NEG	NEG	NEG	
63	GROSS MCHA/LEUCOPENIA,ATYPICAL CELLS/TCP: **PCP**	NEG	NEG	NEG	
64	MACROCYTIC, ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP: **PCP**	NEG	NEG	NEG	
65	MCHA, TARGET CELLS, RETICULOCYTOSIS	NEG	NEG	NEG	
66	MICROCYTIC, HYPOCHROMIC,NORMOCYTIC,ANISOPOIKILOCYTOSIS,TEAR DROP CELLS	NEG	NEG	NEG	
67	MCHA	NEG	NEG	NEG	
68	MCHA/LEUCOPENIA, BLASTS +VE/TCP	NEG	NEG	NEG	
69	MACROCYTIC,ANISOPOIKILOCYTOSIS,TEAR DROP CELLS/HYPERSEGMENTED NEUTROPHILS/TCP: **PCP**	NEG	NEG	NEG	
70	SEVERE MCHA, ANISOPOIKILOCYTOSIS/ LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
71	MACROCYTIC,ANISOPOIKILOCYTOSIS,ERYTHROBLAST/HYPERSEGMENTED NEUTROPHILS/TCP: **PCP**	NEG	NEG	NEG	
72	MACROCYTES/LEUCOPENIA, MYELOID BLAST+ve/TCP: **BICYTOPENIA**	NEG	NEG	NEG	
73	MICROCYTIC,HYPOCHROMIC, RETICULOCYTOSIS/LEUCOPENIA/TCP: **PCP**	NEG	NEG	ANTI HCV +VE	
74	POIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP	NEG	NEG	NEG	
75	MCHA	NEG	NEG	NEG	
76	MYELOID BLAST 85%	NEG	NEG	NEG	
77	ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS,LYMPHOCYTOSIS/TCP	NEG	NEG	NEG	
78	MCHA,TARGET CELLS, RETICULOCYTOSIS	NEG	NEG	HBSAg +VE	
79	MACROCYTIC/LEUCOPENIA	NEG	NEG	NEG	
80	MILD ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/PLATELETE CLUMPS +VE	NEG	NEG	NEG	
81	MACROCYTIC, FEW TARGET CELLS,ANISOPOIKILOCYTOSISI/HYPERSEGMENTED NEUTROPHILS/TCP	NEG	NEG	NEG	
82	MICROCYTIC,HYPOCHROMIC,NORMOCHROMIC RBC	NEG	NEG	NEG	
83	MICROCYTIC,HYPOCHROMIC,NORMOCHROMIC RBC	NEG	NEG	NEG	
84	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	ANA, dsDNA +VE
85	MACROCYTES, ANISOPOIKILOCYTOSIS	NEG	NEG	NEG	
86	ANISOPOIKILOCYTOSIS/HYPERSEGMENTED NEUTROPHILS/TCP: **PCP**	NEG	NEG	NEG	
87	MACROCYTES,ANISOPOIKILOCYTOSIS, ERYTHROBLASTS +ve/HYPERSEGMENTED NEUTROPHILS/TCP	NEG	NEG	NEG	
88	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
89	NORMOCYTIC/RELATIVE LYMPHOCYTOSIS/TCP	DENGUE IgM +VE	NEG	NEG	
90	NCNC/NORMAL WBC/TCP/ P.VIVAX TROPHOIZES +VE RING FORMS	P.VIVAX +	NEG	NEG	
91	NORMOCYTIC,MCHA/TCP	NEG	NEG	NEG	PV DOPPLER: PHT
92	MCHA,ANISOCYTOSIS,PENCIL SHAPED CELLS/LEUCOPENIA,MATURED/TCP: **PCP**	NEG	NEG	NEG	
93	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
94	BLASTS +ve, LEUCOPENIA/TCP	NEG	NEG	NEG	
95	MCHA,ANISOCYTOSIS/LEUCOPENIA,FEW EOSINOPHILS/TCP: **PCP**	NEG	NEG	NEG	
96	DIMORPHIC ANEMIA/ LEUCOPENIA,HYPERSEGMENTED NEUTROPHILS LYMPHOCYTE PREPONDERANCE/ TCP	NEG	NEG	NEG	
97	MCHA/LEUCOPENIA/TCP: **PCP**	NEG	NEG	NEG	
98	MCHA,ELLIPTOCYTOSIS	NEG	NEG	NEG	
99	NCNC/MILD LYMPHOCYTOSIS	NEG	NEG	NEG	
100	MICROCYTIC, HYPOCHROMIC,NORMOCYTIC,ANISOPOIKILOCYTOSIS,TEAR DROP CELLS	NEG	NEG	NEG	

SL. NO	BONE MARROW STUDY	STOOL OCCULT BLOOD	UGI ENDO
1		NEG	NORMAL
2		NEG	
3	BM BX: APLASTIC MARROW	NEG	NORMAL
4	BM BX: HYPOCELLULAR	NEG	
5		NEG	
6	BMA: NO BLAST, BM BX: HYPOCELLULAR WITH TRILINEAGE HEMATOPOIESIS	NEG	
7		NEG	
8	BM BX: HYPOPLASIA	NEG	
9	BM BX: HYPOPLASIA, NO E/O INFILTRATION	NEG	
10	BMA: HYPOCELLULAR, MEGAKARYOCYTES, MICROMEGAKARYOCYTES, MYELOID SERIES NORMAL: **MEGALOBLAST**	NEG	NORMAL
11		NEG	NORMAL
12		NEG	
13	BMA: ERYTHROID HYPERPLASIA/ HISTIOCYTES INCREASED/MEGALOBLASTIC	NEG	
14	BMA: HYPERCELLULAR, INCREASED IRON STORES, BM BX: HYPERCELLULAR, MOD GRANULOCYTIC HYPERPLASIA, M	NEG	NORMAL
15	BM BX:ERYTHROID HYPERPLASIA,	NEG	
16		NEG	
17		NEG	
18		NEG	
19		NEG	
20		NEG	
21	BM BX: GRANULOMATOUS INFLAMMATION	NEG	
22	BMA: HYPOCELLULAR	NEG	
23		NEG	
24		POSITIVE	PANGASTRITIS
25		NEG	
26	HYPERCELLULAR, FRAGMENTED ERYTHROBLAST	NEG	
27	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	
28	HYPERCELLULAR, MEGALOBLASTIC	NEG	NORMAL
29	HYPERCELLULAR,MEGALOBLASTIC, LARGE MEGAKARYOCYTES	NEG	PANGASTRITIS, DUODENITIS
30	IMMATURE MYELOID BLASTS PRESENT	NEG	NORMAL
31		NEG	NORMAL
32	HYPOCELLULAR, REPLACED BY FAT CELLS	POSITIVE	ANTRAL GASTRITIS
33	HYPERCELLULAR, MEGALOBLASTIC, ERYTHROID HYPERPLASIA, LARGE MEGAKARYOCYTES	POSITIVE	ANTRAL GASTRITIS
34		POSITIVE	ESOPHAGEAL VARICES
35		NEG	
36		POSITIVE	ESOPHAGEAL VARICES
37		NEG	
38		NEG	PANGASTRITIS, DUODENITIS
39		NEG	GASTRIC EROSIONS
40	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	
41	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	
42	LEUKEMIC BLASTS +VE	NEG	
43		POSITIVE	PANGASTRITIS, DUODENITIS
44		NEG	
45	NORMOCELLULAR, PRECURSORS NORMAL	NEG	
46	MILD TO MODERATE MEGALOBLASTIC CHANGES	NEG	ESOPHAGEAL VARICES
47		POSITIVE	ESOPHAGEAL VARICES
48	HYPERCELLULAR, DYSERYTHROPOIETIC, ABNORMAL MEGAKARYOCYTES, RINGED SIDEROBLAST	NEG	
49	HYPERCELLULAR, LARGE MEKARYOCYTES +	NEG	NORMAL
50	HYPOCELLULAR,OCC MEGAKARYOCYTES WITH BARE NUCLEI, DYSERYTHROPOIESIS, DECREASE IN ERYTHROID AND	NEG	NORMAL
51	HYPOCELLULAR MARROW, REPLACED BY FAT	NEG	NORMAL
52	HYPERCELLULAR MARROW, NORMAL PRECURSORS	POSITIVE	ESOPHAGEAL VARICES
53	HYPOCELLULAR, FIBROSIS, DECREASED MYELOID PRECURSORS	NEG	NORMAL
54	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	
55		NEG	NORMAL
56	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	NORMAL
57		NEG	NORMAL
58	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	NORMAL
59		NEG	GASTRIC EROSIONS
60	HYPERCELLULAR, MEGALOBLASTIC	NEG	NORMAL
61		NEG	
62	HYPERCELLULAR, MEGALOBLASTIC	NEG	ATROPHIC GASTRITIS
63	HYPERCELLULAR,DYSERYTHROPOIETIC, BINUCLEATED ERYTHROID PRECURSOR, ABNORMAL MEGAKARYOCYTES	NEG	
64	HYPERCELLULAR,MEGALOBLASTIC, ERYTHROID HYPERPLASIA	NEG	NORMAL
65		POSITIVE	ESOPHAGEAL & FUNDAL VARICES
66	HYPERCELLULAR, MEGALOBLASTIC, ERYTHROID HYPERPLASIA	NEG	
67	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	
68	LYMPHOID LEUKEMIC BLASTS PRESENT	NEG	
69		NEG	PANGASTRITIS, DUODENITIS
70	HYPOCELLULAR MARROW, REPLACED BY FAT	NEG	
71	HYPERCELLULAR, MEGALOBLASTIC, METAMYELOCYTES +VE	NEG	NORMAL
72	HYPERCELLULAR, MEGALOBLASTIC	NEG	
73		POSITIVE	ESOPHAGEAL VARICES
74	HYPERCELLULAR, MEGALOBLASTIC	NEG	NORMAL
75		POSITIVE	ESOPHAGEAL VARICES
76	MYELOID LEUKEMIC BLAST	NEG	
77		NEG	PANGASTRITIS
78	HYPERCELLULAR, NORMAL PRECURSORS	POSITIVE	ESOPHAGEAL & GASTRIC VARICES
79	HYPOCELLULAR MARROW, REPLACED BY FAT	NEG	NORMAL
80		POSITIVE	EROSIVE GASTRITIS
81		NEG	EROSIVE GASTRITIS
82	HYPERCELLULAR MARROW, RINGED SIDEROBLAST +ve, DYSPLASTIC	NEG	
83	HYPOCELLULAR MARROW	NEG	NORMAL
84	HYPOCELLULAR MARROW, REPLACED BY FAT	NEG	NORMAL
85	HYPERCELLULAR, MEGALOBLASTIC	NEG	NORMAL
86		NEG	ATROPHIC GASTRITIS
87		NEG	GASTRITIS
88	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	
89		NEG	
90		NEG	
91		NEG	ESOPHAGEAL VARICES
92		NEG	
93	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	
94	LYMPHOID LEUKEMIC BLASTS PRESENT	NEG	
95	HYPOCELLULAR, BONE MARROW HYPOPLASIA	NEG	
96		NEG	
97	HYPOCELLULAR, REPLACED BY FAT CELLS	NEG	
98		POSITIVE	ESOPHAGEAL VARICES, GASTRITIS
99	NORMOCELLULAR, PRECURSORS NORMAL	NEG	
100	HYPERCELLULAR, MEGALOBLASTIC, ERYTHROID HYPERPLASIA	NEG	

SL NO.	BONE MARROW STUDY	DIAGNOSIS	S. IRON	S. FERRITIN
1		APLASTIC ANEMIA		
2		MEGALOBLASTIC ANEMIA; VIT B12 DEF.		
3	BM BX: APLASTIC MARROW	APLASTIC ANEMIA		
4	BM BX: HYPOCELLULAR	FANCONI ANEMIA		
5		P. VIVAX MALARIA		
6	BMA: NO BLAST, BM BX: HYPOCELLULAR WITH TRILINEAGE HEMATOPOIESIS	APLASTIC ANEMIA		
7		MEGALOBLASTIC ANEMIA; FOLATE DEF.		
8	BM BX: HYPOPLASIA	APLASTIC ANEMIA		
9	BM BX: HYPOPLASIA, NO E/O INFILTRATION	APLASTIC ANEMIA		
10	BMA: HYPOCELLULAR, MEGAKARYOCYTES, MICROMEGAKARYOCYTES, MYELOID SERIES NORMAL: **MEGALOBLAST**	MDS/MEGALOBLASTIC ANEMIA		
11		MEGALOBLASTIC ANEMIA; VIT B12 & FOLATE DEF.		
12		P. VIVAX MALARIA		
13	BMA: ERYTHROID HYPERPLASIA/ HISTIOCYTES INCREASED/MEGALOBLASTIC	MEGALOBLASTIC ANEMIA; VIT B12 & FOLATE DEF, CLD WITH PHT		
14	BMA: HYPERCELLULAR, INCREASED IRON STORES, BM BX: HYPERCELLULAR, MOD GRANULOCYTIC HYPERPLASIA, M	MDS		
15	BM BX:ERYTHROID HYPERPLASIA,	APLASTIC ANEMIA		
16		MEGALOBLASTIC ANEMIA; VIT B12 & FOLATE DEF.		
17		MEGALOBLASTIC ANEMIA; VIT B12 & FOLATE DEF.		
18		SLE		
19		DENGUE FEVER		
20		MEGALOBLASTIC ANEMIA: FOLATE DEF.		
21	BM BX: GRANULOMATOUS INFLAMMATION	DISSEMINATED TB		
22	BMA: HYPOCELLULAR	APLASTIC ANEMIA		
23		P. VIVAX MALARIA		
24		HYPERSPLENISM		
25		MEGALOBLASTIC ANEMIA: VIT B12 DEF.		
26	HYPERCELLULAR, FRAGMENTED ERYTHROBLAST	MDS	170	250
27	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
28	HYPERCELLULAR, MEGALOBLASTIC	MEGALOBLASTIC ANEMIA: VIT B12 DEF.	250	185
29	HYPERCELLULAR,MEGALOBLASTIC, LARGE MEGAKARYOCYTES	MEGALOBLASTIC ANEMIA:FOLATE DEF.	117	234
30	IMMATURE MYELOID BLASTS PRESENT	ACUTE MYELOID LEUKEMIA	199	175
31		MEGALOBLASTIC ANEMIA: VIT B12 DEF.	211	197
32	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
33	HYPERCELLULAR, MEGALOBLASTIC, ERYTHROID HYPERPLASIA, LARGE MEGAKARYOCYTES	MEGALOBLASTIC ANEMIA		
34		HYPERSPLENISM, EHPVO, CLD	120	95
35		DENGUE FEVER		
36		HYPERSPLENISM, NCPF		
37		MEGALOBLASTIC ANEMIA: VIT B12 DEF.	256	195
38		MEGALOBLASTIC ANEMIA: VIT B12 DEF.	171	288
39		MEGALOBLASTIC ANEMIA: VIT B12 DEF.	345	256
40	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
41	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
42	LEUKEMIC BLASTS +VE	ACUTE MYELOID LEUKEMIA		
43		MEGALOBLASTIC ANEMIA: VIT B12 DEF.	231	340
44		MEGALOBLASTIC ANEMIA: FOLATE DEF./HYPOTHYROID	185	213
45	NORMOCELLULAR, PRECURSORS NORMAL	VIRAL INDUCED PANCYTOPENIA		
46	MILD TO MODERATE MEGALOBLASTIC CHANGES	HYPERSPLENISM/CLD/HCV	95	154
47		HYPERSPLENISM, CLD, ETHANOL	138	98
48	HYPERCELLULAR, DYSERYTHROPOIETIC, ABNORMAL MEGAKARYOCYTES, RINGED SIDEROBLAST	MDS	176	262
49	HYPERCELLULAR, LARGE MEKARYOCYTES +	MEGALOBLASTIC ANEMIA,VIT B12 DEF., HYPOTHYROID	250	176
50	HYPOCELLULAR,OCC MEGAKARYOCYTES WITH BARE NUCLEI, DYSERYTHROPOIESIS, DECREASE IN ERYTHROID AND	HIV INDUCED PANCYTOPENIA	79	55
51	HYPOCELLULAR MARROW, REPLACED BY FAT	APLASTIC ANEMIA		
52	HYPERCELLULAR MARROW, NORMAL PRECURSORS	HYPERSPLENISM, EHPVO	87	98
53	HYPOCELLULAR, FIBROSIS, DECREASED MYELOID PRECURSORS	SLE, CTD		
54	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
55		MEGALOBLASTIC ANEMIA: VIT B12 DEF.	199	280
56	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
57		MEGALOBLASTIC ANEMIA, FOLATE DEF.	160	153
58	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
59		MEGALOBLASTIC ANEMIA, VIT B12 DEF.	163	251
60	HYPERCELLULAR, MEGALOBLASTIC	MEGALOBLASTIC ANEMIA, VIT B12 & FOLATE DEF.	204	190
61		DENGUE		
62	HYPERCELLULAR, MEGALOBLASTIC	MEGALOBLASTIC ANEMIA: VIT B12 DEF.	168	176
63	HYPERCELLULAR,DYSERYTHROPOIETIC, BINUCLEATED ERYTHROID PRECURSOR, ABNORMAL MEGAKARYOCYTES	MDS		
64	HYPERCELLULAR,MEGALOBLASTIC, ERYTHROID HYPERPLASIA	MEGALOBLASTIC ANEMIA: VIT B12 DEF.	234	170
65		HYPERSPLENISM, EHPVO	55	101
66	HYPERCELLULAR, MEGALOBLASTIC, ERYTHROID HYPERPLASIA	MEGALOBLASTIC ANEMIA	134	156
67	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
68	LYMPHOID LEUKEMIC BLASTS PRESENT	ALL		
69		MEGALOBLASTIC ANEMIA: VIT B12 DEF.	180	284
70	HYPOCELLULAR MARROW, REPLACED BY FAT	APLASTIC ANEMIA		
71	HYPERCELLULAR, MEGALOBLASTIC, METAMYELOCYTES +VE	MEGALOBLASTIC ANEMIA, VIT B12 DEF.	160	170
72	HYPERCELLULAR, MEGALOBLASTIC	MEGALOBLASTIC ANEMIA, VIT B12 DEF.		
73		HYPERSPLENISM, CLD, HCV		
74	HYPERCELLULAR, MEGALOBLASTIC	MEGALOBLASTIC ANEMIA, VIT B12 DEF.		
75		HYPERSPLENISM, CLD, ETHANOL	65	90
76	MYELOID LEUKEMIC BLAST	ACUTE MYELOID LEUKEMIA		
77		MEGALOBLASTIC ANEMIA, FOLATE DEF.	235	305
78	HYPERCELLULAR, NORMAL PRECURSORS	HYPERSPLENISM, CLD, HBV	75	105
79	HYPOCELLULAR MARROW, REPLACED BY FAT	APLASTIC ANEMIA		
80		MEGALOBLASTIC ANEMIA, VIT B12 DEF.	180	294
81		MEGALOBLASTIC ANEMIA	176	355
82	HYPERCELLULAR MARROW, RINGED SIDEROBLAST +ve, DYSPLASTIC	MDS		
83	HYPOCELLULAR MARROW	SLE, CTD	87	189
84	HYPOCELLULAR MARROW, REPLACED BY FAT	APLASTIC ANEMIA		
85	HYPERCELLULAR, MEGALOBLASTIC	MEGALOBLASTIC ANEMIA, FOLATE DEF.	176	188
86		MEGALOBLASTIC ANEMIA, VIT B12 DEF.	134	120
87		MEGALOBLASTIC ANEMIA, VIT B12 DEF.	175	299
88	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
89		DENGUE		
90		P. VIVAX MALARIA		
91		HYPERSPLENISM, CLD		
92		NCPF		
93	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
94	LYMPHOID LEUKEMIC BLASTS PRESENT	ALL		
95	HYPOCELLULAR, BONE MARROW HYPOPLASIA	TOULENE INDUCED APLASIA, VIT B12 DEF.		
96		MEGALOBLASTIC ANEMIA: VIT B12 & FOLATE DEF.		
97	HYPOCELLULAR, REPLACED BY FAT CELLS	APLASTIC ANEMIA		
98		HYPERSPLENISM,CLD		
99	NORMOCELLULAR, PRECURSORS NORMAL	VIRAL INDUCED PANCYTOPENIA		
100	HYPERCELLULAR, MEGALOBLASTIC, ERYTHROID HYPERPLASIA	MEGALOBLASTIC ANEMIA	130	150